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Original Communications

THE ROLE OF CESAREAN SECTION IN THE TREATMENT OF PREMATURE SEPARATION OF THE NORMALLY IMPLANTED PLACENTA*

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IN 1870 Goodell[1] laid down as the principles of treatment for premature separation of the normally implanted placenta the dictum of Theodore Mayern that the uterus should be evacuated as soon as possible ("Praestantissimum remedium est foetus extractio"). Cesarean section has always appealed to the obstetrician as the most effective and rapid method of accomplishing this end. In the early days, however, patients were brought to the hospital after many hours of labor and in a state of shock so that all of the earlier writers reported high mortality rates for cesarean section as opposed to the vaginal method of delivery.

During recent years many factors have combined to reduce the dangers of cesarean section. The most important of these is the adoption of a carefully individualized anesthesia, given by the most skilled anesthetists available. Of equal importance is also the modern attitude toward operation in shock. It has been found that prompt and repeated transfusions can place an otherwise desperate patient in satisfactory condition to withstand operation.

In 1870 Goodell wrote "by far the most frequent symptom is an alarming state of collapse." This is not true today for there are many communities, in which my own is included, where prenatal care is all

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but universally given by physicians who are well acquainted with the danger signs of bleeding in the last trimester of pregnancy. In my community, as in many others, hospitalization of obstetric patients is practically universal, and transportation to the hospital is quickly accomplished. In 1890 Holmes[2] wrote, "Cesarean section will be of value in selected cases, but never will be popular, for the conditions and surroundings favoring celiotomy will seldom be at hand." This is no longer true in my community.

Notwithstanding recent papers by DeNormandie,[3] McGlinn and Harer,[4] Falls,[5] Montgomery,[6] and Stander,[7] we find that Irving,[8] and Holmes,[9] as late as 1937 and 1940, respectively, considered cesarean section as a dangerous method of delivery compared with the vaginal methods, and voiced the opinion that hysterectomy in such cases greatly increases the mortality. Holmes quotes Irving's tables showing 4.9 per cent mortality for the conservative type treatment as against 16.8 per cent mortality for cesarean section, and Irving in his review of the subject gives a mortality of 2.9 per cent for conservative as against 14.5 per cent for the cesarean method. Irving further states that since giving up the use of cesarean sections for this purpose at the Boston Lying-in Hospital there has been only one death since 1931. He quotes DeSnoo who gives 6 per cent mortality for the conservative treatment as against 33 per cent for the more radical method in cases where the placenta has about half separated.

I wish to protest against such use of mortality figures. This is not justified for two reasons: First, no account has been taken of improvement in the matter of transfusions and anesthesia; and second, it is obvious that cesarean sections, and especially hysterectomies, were done in the more serious type of case. Comparing such operative mortalities with those of the vaginal deliveries, where many cases of minor degree are included, is a fundamental statistical error. We have learned from studies of the end results of cancer treatment that we must compare groups of cases which, at the beginning of treatment, have arrived at similar stages of the disease, otherwise the comparisons of the results of one clinic with another are quite meaningless. The same holds true in this discussion.

The attitude of obstetricians at the Hartford Hospital is in line with that advocated by McGlinn and Harer,[4] which is briefly as follows: Delivery by the vaginal route is warranted only when delivery is actually immediately impending or may be promptly accomplished by use of an obstetrical maneuver. In all other cases cesarean section is indicated. Stander[7] puts it as follows: "most cases . . . except those in which the cervix is dilated and delivery can be quickly accomplished should be subjected to cesarean section." As will be seen from the various tables which follow, death of the fetus is not considered a contraindication to cesarean section. We believe that cesarean section is best used very early, as soon as the diagnosis is made, before the condition of the patient and of the uterus has become grave and if possible before the baby has died.

It is obvious that clinics where most of the patients are brought in late in labor, and in bad condition, have been prejudiced against cesarean section and in favor of vaginal methods. Teachers of obstetrics who are preparing practitioners for home deliveries will accent those maneuvers which the practitioner must know how to perform in the absence of ideal surroundings. We believe, however, that the deliberate choice of the vaginal method of delivery early in labor and where ideal surroundings are present is justified neither by our clinical experience nor by our understanding of the progressively malignant process which is going on in the uterus.

MATERIAL

The present review is a study of 120 cases which have been found on careful search of the records of the Hartford Hospital from Oct. 1, 1916, to Oct. 1, 1940. These dates were chosen because my experience in the hospital covered this period and my previous studies of hospital histories have been made on admissions since 1916. In all fairness it should be said at the outset that one death following cesarean section done for premature separation of the placenta is recorded in the year 1914. This is the only such death in the hospital's cesarean section experience. The patient was severely toxic, was operated upon by an interne under staff supervision, while in shock, with gas-oxygen-ether anesthesia. Both the mother and baby died, the mother surviving the operation by two hours. Prior to 1916 adequate records do not permit statistical study in this field. During the years covered by this study, hospital deliveries increased from 985 to 2,371 per year. Eleven hundred and sixty-two cesarean sections were performed from 1927 to 1940: 4.6 per cent for placenta previa and 4.7 per cent for premature separation of the placenta. During the last nine years the incidence of cesarean section for the whole clinic was 5.0 per cent, and the mortalities for 883 cesarean sections was 0.68 per cent. Since the last death after cesarean section, there have been, up to Oct. 1, 1940, 332 consecutive cesarean sections without a death. It will be appreciated, therefore, that cesarean section is done on very liberal indications. While it is undoubtedly true that some of the cesarean sections done for premature separation might have been avoided in favor of vaginal delivery, adverse criticism cannot be based on our mortality record.

Table I is a synopsis of the individual case histories. It will be noted from the hospital history serial numbers that the use of cesarean section, especially in the more serious cases, is a development of the more recent years. It will be noted that very few such diagnoses were made prior to 1926, the histories of which period are numbered below 200,000. For the years prior to 1926 all cases which had cesarean sections are listed, whereas it is probable that many of the milder cases delivered by the vaginal route failed to be included. The omission of these cases prior to 1926 does not materially change the enumerations. This table arranges the cases in what we believe to be the order of their severity, giving primary consideration to the estimate of the degree of separation. The scale of one to four is used in which one is the least and four the greatest. The secondary items of arrangement concern the estimated blood loss, shock, the degree of rigidity, and in cesarean section cases the degree of apoplexy. In the absence of such accurate data as those

TABLE I*

CESAREAN SECTIONS (59)											VAGINAL DELIVERIES (61)									
HISTORY NUMBER	SEPARATION	BLOOD LOSS	SHOCK	RIGIDITY	APOPLEXY	TOXEMIA	BABY	AGE	GRAVIDA	PARA	HISTORY NUMBER	SEPARATION	BLOOD LOSS	SHOCK	RIGIDITY	TOXEMIA	BABY	AGE	GRAVIDA	PARA
302973	4	3	4	0	3	0	SB	23	1	0	198796	4	4	4	4	0	SB	34	2	1
275539	4	3	3	3	4	0	SB	18	1	0	380959	4	3	1	?	0	SB	39	7	4
395456	4	3	3	3	4	0	SB	25	1	0	206764	4	2	1	2	0	SB	18	1	0
350751	4	3	3	4	2	?	SB	40	13	10	238126	4	2	0	4	ECL	SB	35	3	2
334078	4	3	3	?	1	0	SB	36	3	2	373128	4	2	0	0	1	SB	30	3	0
301501	4	3	2	0	3	2	SB	33	2	1	349719	4	2	0	0	?	SB	18	1	0
338648	4	3	0	4	2	3	SB	41	6	3	368412	4	1	0	0	0	SB	23	1	0
330660	4	3	0	4	2	0	SB	31	3	2	220077	3	3	0	3	0	SB	34	4	3
209568	4	2	0	4	2	2	SB	37	5	4?	393541	3	2	0	0	0	SB	33	3	2
367329	4	2	0	4	2	2	SB	30	1	0	200050	3	2	0	0	0	NN	30	6	5
336836	4	2	0	4	2	0	SB	28	3	2	236883	3	1	0	4	4	SB	37	7	?
266185	4	2	0	?	1	0	SB	32	3	2?	238131	2	3	0	2	0	SB	37	9	?
345707	3	3	2	4	2	0	SB	27	2	1	374116	2	2	0	0	0	L	22	1	0
301516	3	3	2	0	2	1	SB	25	1	0	293360	2	2	0	0	0	L	28	3	2
190241	3	3	0	4	3	0	SB	43	10	8	219135	2	2	0	0	0	SB	31	6	5?
309093	3	2	0	3	0	0	SB	27	3	2	356988	2	1	0	2	0	L	24	3	2
251247	3	2	0	3	0	0	SB	37	4	3	348922	2	1	0	0	ECL	SB	26	1	0
337193	3	2	0	2	2	0	SB	38	1	0	345403	1	3	0	0	0	L	22	1	0
321980	3	2	0	0	1	0	SB	36	3	2	369983	1	2	0	0	0	L	29	1	0
284842	2	3	2	4	0	?	L	32	7	5	395806	1	2	0	0	0	L	31	2	1
271346	2	3	0	1	2	0	SB	21	3	2	328296	1	2	0	0	0	L	28	2	1
397032	2	2	2	0	2	1	SB	36	7	4	325741	1	2	0	0	?	L	30	4	3
353462	2	2	1	4	2	0	L	31	1	0	328931	1	2	0	0	0	L	35	3	2
212284	2	2	1	?	?	0	L	26	1	0	314126	1	1	0	0	2	L	36	1	0
274529	2	2	0	3	2	1	L	33	2	0	271127	1	1	0	0	2	L	22	1	0
379874	2	2	0	2	0	0	L	38	3	?	373517	1	1	0	0	0	L	31	1	0

275004	2	2	0	2	0	0	L	27	3	2	220807	1	1	0	0	0	NN	27	4	3?
370781	2	2	0	1	?	0	L	30	1	0	286634	1	1	0	0	0	SB	25	1	0
331515	2	2	0	0	1	2	L	26	1	0	300255	1	1	0	0	0	SB	30	1	0
378021	2	2	0	0	0	0	L	37	2	1	218511	1	1	0	0	0	L	25	2	1
255706	2	2	0	0	0	0	NN	21	1	0	234491	1	1	0	0	0	L	25	2	1
331855	2	2	0	?	2	0	L	32	2	1	356954	1	1	0	0	0	L	32	2	1
241144	2	2	0	?	1	0	L	26	1	0	373368	1	1	0	0	0	L	35	2	1
173384	2	2	0	?	0	1	L	30	1	0	346340	1	1	0	0	0	L	31	2	1
393804	2	1	0	2	2	3	L	25	3	2	242244	1	1	0	0	0	L	21	1	0
349193	2	1	0	0	1	0	L	23	1	0	313899	1	1	0	0	0	L	30	4	3
358600	2	1	0	0	0	0	L	32	5	1	239463	1	1	0	0	0	L	29	3	2
366943	1	2	2	0	0	0	SB	36	3	2	354334	1	1	0	0	3	L	24	1	0
311567	1	2	0	2	2	0	L	25	1	0	260996	1	1	0	0	3	L	36	2	1
320741	1	2	0	0	2	0	L	27	1	0	393520	1	1	0	0	0	L	33	1?	0
100164	1	2	0	0	0	0	L	28	1	0	393135	1	1	0	0	0	L	24	1	0
226279	1	2	0	0	0	0	NN	23	1	0	385786	1	1	0	0	0	L	?	2	1?
368419	1	2	0	0	0	0	L	27	2	?	393182	1	1	0	0	0	L	41	11	7
135491	1	2	0	0	0	0	L	32	2	1	393635	1	1	0	0	0	L	27	1	0
377112	1	2	0	0	0	0	L	33	3	2	267815	1	1	0	0	2	L	29	7	6
319567	1	2	0	0	0	0	L	19	1	0	302722	1	1	0	0	1	L	34	3	2
289984	1	2	0	0	0	1	L	27	2	1	314289	1	1	0	0	0	L	38	10	8
311651	1	1	0	4	0	ECL	L	22	1	0	313895	1	1	0	0	0	NN	33	4	1
248660	1	1	0	2	0	0	L	33	1	0	347043	1	?	0	0	0	L	30	2	1
387922	1	1	0	2	0	0	L	26	1	0	388893	1	?	0	0	0	L	30	2	1
396638	1	1	0	2	0	0	L	29	3	1	211267	1	?	0	0	0	L	22	3	1
381632	1	1	0	0	0	?	L	28	2	1	383091	?	2	0	0	0	L	21	1	0
213566	1	1	0	0	0	0	SB	35	1	0	309685	?	2	0	0	?	SB	28?	5	3
312607	1	1	0	0	0	2	L	33	1	0	383657	?	1	0	0	0	L	34	1	0
260748	1	?	0	0	0	3	NN	35	5	4	369140	?	1	0	0	0	NN	24	1	0
347005	?	4	1	?	2	0	SB	26	1	0	288925	?	1	0	0	0	NN	31	1	0
275449	?	2	2	?	0	2	L	17	1	0	274215	?	1	0	0	0	L	37	2	1
327861	?	?	0	3	0	0	L	22	1	0	285905	?	1	0	0	2	SB	27	2	1
318661	?	2	0	0	0	0	L	35	1	0	113860	?	?	?	3	?	SB	?	5	4
											391901	?	?	0	0	0	SB	25	1	0
											121652	?	?	?	?	4	SB	28	7	6

*SB, signifies stillbirth; NN, neonatal death; L, discharged alive; ECL, eclampsia; ?, insufficient data.

who work in University clinics are accustomed to find, it is obvious that certain errors in assigning the degree of severity for all these factors may creep in. Sufficient records, however, were available to furnish a shrewd guess for the purposes of this study.

Table II summarizes Table I and clearly shows that in all enumerations, except toxemia, the more serious cases tended to be handled by cesarean section and the less serious by the vaginal route.

TABLE II. PREMATURE SEPARATION OF THE PLACENTA, HARTFORD HOSPITAL 1916-1940
Comparison (by Grades) of Cesarean Section vs. Vaginal Deliveries

GRADES	VAGINAL	CESAREAN
	Separation	
4	7	12
3	4	7
2	6	18
1	34	18
?	10	4
	61	59
	Blood Loss	
4	1	1
3	4	13
2	16	34
1	33	10
?	7	1
	61	59
	Shock	
4	1	1
3	0	4
2	0	7
1	2	3
0	56	44
?	2	0
	61	59

GRADES	VAGINAL	CESAREAN
	Rigidity	
4	3	11
3	2	6
2	1	8
1	0	2
0	53	24
?	2	8
	61	59
	Toxemia	
Ecl.	2	1
4	2	0
3	2	3
2	4	6
1	2	5
0	45	44
?	4	0
	61	59

Table III shows the division according to the number of pregnancies and the duration of gestation.

TABLE III. PREMATURE SEPARATION OF THE PLACENTA
HARTFORD HOSPITAL 1916-1940

Total 120	Private 79	Ward 41	
Gravida i			50
Gravida ii-v			54
Gravida vi and over			16
Gestation up to 28 wk.			9
Gestation 29 to 31 wk.			2
Gestation 32 to 35 wk.			21
Gestation 36 and over			83
Not stated			5

Table IV shows the number of the various grades of toxemia. It is highly probable that, in the five instances where toxemia was not stated, the degree was either "zero" or "one." It would seem from this table that private patients received closer prenatal supervision than ward cases.

TABLE IV. PREMATURE SEPARATION OF THE PLACENTA

HARTFORD HOSPITAL 1916-1940

Toxemia Grade	0	88
	1	7
	2	10
	3	5
	4	5
Not stated		5
Eclampsia		3
Private cases with no toxemia		90%
Ward cases with no toxemia		70%

Tables V and VI attempt to analyze the relationship between toxemia and hemorrhagic infiltration of the uterine muscle in cesarean sections. It is clearly evident that severe toxemia, in our experience, has played a very small part in the production of the uterine lesion.

Table VII shows comparison of the fetal loss by the two methods of delivery according to the degree of separation of the placenta. For

TABLE V. PREMATURE SEPARATION OF PLACENTA, HARTFORD HOSPITAL 1916-1940

Cesarean sections 59 Toxic 15

TOXEMIA GRADE	APOPLEXY GRADE					
	0	1	2	3	4	TOTAL
0	24	5	11	2	2	44
1	2	0	3	0	0	5
2	2	1	2	1	0	6
3	1	0	2	0	0	3
4	0	0	0	0	0	0
Eclampsia	1	0	0	0	0	1
	30	6	18	3	2	59

TABLE VI. PREMATURE SEPARATION OF PLACENTA, HARTFORD HOSPITAL 1916-1940

Cesarean sections 59. Apoplexy (hemorrhagic infiltration of uterine muscle) 29

APOPLEXY GRADE	WITH TOXEMIA	NONTOXIC
1	1	5
2	7	11
3	1	2
4	0	2
	9	20

TABLE VII. PREMATURE SEPARATION OF THE PLACENTA, HARTFORD HOSPITAL 1916-1940

Fetal Loss by Cesarean Section vs. Vaginal Deliveries
(By Degree of Separation of the Placenta)

DEGREE OF SEPARATION	METHOD OF DELIVERIES		LIVE BABIES		STILLBIRTHS		NEONATAL DEATHS	
	C.S.	VAG.	C.S.	VAG.	C.S.	VAG.	C.S.	VAG.
1	18	35	14	30	2	3	2	2
2	18	6	15	3	2	3	1	0
3	7	4	0	0	7	3	0	1
4	12	7	0	0	12	7	0	0
?	4	9	3	3	1	4	0	2
Totals	59	61	32	36	24	20	3	5

this series there is very little difference in the number of live babies which were discharged from the hospital after the neonatal period. It is also evident, as it was in Table I, that cesarean sections were done more frequently in the serious cases.

Table VIII shows the comparison of our cases with those of the Boston Lying-in Hospital, published by Goethals.[10] A strict comparison of these two series should not be made, for the greater number of the Hartford Hospital group was handled in the fourteen years after the Boston series ended. The number of primiparas in our series is appreciably greater. The periods of gestation and the number of nontoxic cases are almost identical. The greater number of eclampsia, cesarean section deaths, fetal deaths, maternal mortality, and severe degrees of detachment and rigidity in the Boston series undoubtedly indicate to some extent the greater severity of the cases in the early period.

TABLE VIII. PREMATURE SEPARATION OF THE PLACENTA, HARTFORD HOSPITAL 1916-1940

Boston Lying-in Hospital and Hartford Hospital Series Compared

	B.L.-I. 1916-26	H.H. 1916-40
Total	128	120
Gravida i	39	50
36 weeks +	85	83
Nontoxic	91	88
Eclampsia	6	3
Cesarean section (deaths)	39-(3)	59-(0)*
Rigidity (3 and 4)	42	22
Detachment (4)	35	21
Mothers died	11	2
Fetus died	80	52

*One death after cesarean section in 1914. (The only such death in the Hartford Hospital cesarean history.)

Objection can be raised against the use of cesarean section where vaginal delivery might be employed on the score that subsequent childbearing will be diminished. Table IX shows that our experience in this regard does not bear out such criticism. Whatever limitation to subsequent childbearing might have been caused by the employment of cesarean section, there was still greater loss of subsequent productive fertility in cases where cesarean section was not employed.

TABLE IX. PREMATURE SEPARATION OF THE PLACENTA, HARTFORD HOSPITAL 1916-1940

Subsequent Pregnancies in Patients Delivered as Shown Prior to Oct. 1, 1939. Comparing Cesarean vs. Vaginal Deliveries

	CESAREAN SECTION	VAGINAL
Total	49	51
Hysterectomies	6	0
Sterilized	1	0
Possibly fertile	42	51
No known pregnancies	29	41
Subsequently pregnant	13	10
Subsequent pregnancies	17	11
Live babies	13	7
Subsequent cesarean section	11	2
Subsequent premature separation	3	3

Objection to the cesarean method may be raised also on the score of danger of rupture of the uterine scar in subsequent pregnancies. The records of all subsequent pregnancies were studied and in only one instance was there observed a poorly healed uterine incision. [In that instance I had personally sutured the uterus with care. The uterus was not hemorrhagic in any degree, nor was the patient toxic, and the failure of adequate healing cannot in my opinion be ascribed to anything but the cesarean method.] In this case, however, a subsequent cesarean section was done at the time of election without a rupture of the uterus, and a live baby was obtained.

MORTALITY

The two deaths recorded in this series were of patients who were delivered by the vaginal method. A synopsis of these cases is given.

CASE 1.—In 1920 a private case of a general practitioner, gravida vii, para vi, 28 years of age. She bled severely on admission and after delivery. Her total labor lasted six hours. She was packed before admission, following which the packing was removed, bag inserted and manual dilatation was performed. A stillborn fetus was delivered spontaneously under chloroform anesthesia. The patient died on the fourth day, her temperature having risen to more than 100.4° F. on one day only. Albumin and casts were present in large amounts, and she died with the appearance of cardiac decompensation with pulmonary edema.

CASE 2.—The second patient, gravida ii, para i, 34 years of age, was delivered in 1927 (private case of an obstetrician). She came in promptly after the onset of pains which awakened her from sleep. The pains were accompanied by considerable blood loss. On admission the cervix was dilated manually from one to three fingers. The edge of the placenta was felt and the membranes were ruptured, allowing the head to descend. Bleeding then stopped. It was noted, however, that the uterus was boardlike, and when she delivered spontaneously (six hours after onset of labor), a stillborn baby and placenta were extruded with a very large amount of fluid and clotted blood. In spite of uterine tamponade which was carried out twice, the patient died (ten hours after the first pains) before a transfusion could be arranged. The diagnosis in this case was both a placenta previa marginalis and premature separation of the low-lying placenta. An autopsy was not obtained.

This second death recalls the cases presented by Rudolph[11] in which he was able to observe at cesarean section a typical hemorrhagic uterus and found the placenta attached to the lower posterior wall. Not only Rudolph but Montgomery[6] and Kellogg[12] report that numerous such instances of premature separation with low-lying placenta are encountered. Such cases raise the question as to whether the classical definition of this condition is fully justified. I do not agree, however, with Montgomery that these cases with retroplacental hematomas, spasm of the uterus, and hemorrhage in the muscle should be called placenta previa.*

In his paper on "Ablatio Placentae," Holmes[9] said "failure to find the placenta within reach of the finger makes the diagnosis certain. In placenta previa the discovery of the afterbirth is positive, no pain so characteristic of ablatio is present, and no distention is met with." His definition recognizes only anatomic boundaries, viz., if the placenta has attached above that portion of the uterus which must dilate, the case is properly called ablatio. It would seem that this definition does not include some of the undoubtedly typical cases.

*It would be convenient for us to use the customary classification, for if we did so our whole series would present no death since 1920.

DISCUSSION

The necessity of removing the uterus has undoubtedly been exaggerated and our group in Hartford is convinced that too many uteri have been removed. The conservative school has shown that hemorrhage seldom persists after the uterus is emptied. We recall, however, the case reported by Frank[13] of a severe Couvelaire uterus emptied by low classical cesarean section. Pituitrin was injected into the uterine muscle and a firm uterine and vaginal pack was later employed which failed to stop the bleeding. Hysterectomy was done six hours after the cesarean section and the patient survived, due undoubtedly to repeated transfusions. Urine and blood pressure were normal.

Some hysterectomies have been done as the easiest way to sterilize where this was desirable. Where the hemorrhagic process has extensively involved the wall of the uterus, it has been removed, having in mind the disastrous results of necrobiosis of the uterine muscle reported by Coventry and Moe.[14]

Since we have been doing cesarean sections very early and have observed the hemorrhagic lesion in the absence of toxemia, trauma or other discernible factors, we have become dissatisfied with the many explanations of etiology which have been advanced, and it is suggested that renewed efforts be made to study the blood vessel lesions not only in the late but in the early cases, making use of recently developed injection and special staining techniques. It is not yet clear why the separation of the placenta within the uterus should cause hemorrhagic infiltration which is invariably confined to the outer and not the inner layers of the uterus. May we not be dealing with a process which should be investigated as a result of isoimmunization reactions, bringing this lesion in line with many spontaneous abortions, miscarriages, and unexplained fetal deaths, and perhaps with erythroblastosis fetalis? (Levine, Katzin, Burnham.[15])

CONCLUSIONS

1. Indications for cesarean section in the treatment of premature separation of the normally implanted placenta should be extended wherever ideal conditions are obtainable.

2. Under ideal surroundings cesarean section, even in the presence of shock, can be safely employed, provided adequate methods are used to combat shock by transfusions and fluid administration, and provided the operation is skillfully performed under expertly administered anesthesia which is suited to the patient's needs.

3. Experience of the Hartford Hospital over many years has shown that cesarean section can be employed without increase in mortality and without severely limiting subsequent childbearing, and further that in the presence of a live child, fetal losses are greatly diminished.

4. Attention is called to the inadequacy of a purely anatomic division between premature separation of the normally implanted placenta and placenta previa.

5. Hope is expressed that observation of early lesions with study of the vascular lesions by modern methods may furnish us with a clearer understanding of etiology.

REFERENCES

(1) *Goodell, W.:* Am. J. Obst. 2: 281, 1870. (2) *Holmes, R. W.:* Am. J. Obst. 44: 753, 1901. (3) *DeNormandie, R. L.:* Am. J. Obst. & Gynec. 31: 325, 1936. (4) *McGlinn, J. A., and Harer, W. B.:* Ibid. 30: 226, 1935. (5) *Falls, F. H.:* Journal-Lancet 54: 107, 1934. (6) *Montgomery, T. L.:* Discussion of DeNormandie's paper q.v. (7) *Stander, H. J.:* Curtis' Obstetrics and Gynecology 2: 445, Philadelphia, 1934, W. B. Saunders Co. (8) *Irving, F. C.:* Int. Abst. Surg. 67: 56, 1938. (9) *Holmes, R. W.:* Am. J. Surg. 48: 61, 1940. (10) *Goethals, T. R.:* Am. J. Obst. & Gynec. 15: 627, 1928. (11) *Rudolph, L.:* Ibid. 32: 479, 1936. (12) *Kellogg, F. S.:* Ibid. 15: 357, 1928. (13) *Frank, C. W.:* Ibid. 33: 512, 1937. (14) *Coventry, W. A., and Moe, R. J.:* Ibid. 25: 859, 1933. (15) *Levine, P., Katzin, E. M., and Burnham, L.:* J. A. M. A. 116: 825, 1941.

DISCUSSION

DR. RUDOLPH W. HOLMES, University, Va.—Those who have written on ante-partum placental separation have erected a structure of hypotheses elaborated from presumptive evidence, and based upon conjectural notions as to the etiology. Truth will be derived only when there shall be a discovery of the specific etiologic factors. Dr. Miller and I disagree on many fundamentals. In fact, the tenor of his paper, reflecting the experience and observation of the Hartford Hospital Staff, tends to controvert the prevalent concepts held by most authorities.

An analysis of his tables reveals that practically all of his cases were definitely benign, in sharp contrast to the tragic cases reported by most writers on the subject. It is noteworthy that there is an entire absence of the tetrad in any single patient of severe toxemia, severe hemorrhage, excessive shock and complete placental separation. He makes no mention of excessive distention or severe uterine pain, which are both characteristic of ablatio. Toxemia was noted in only 27 (23.9 per cent) of his 120 case reports. No mention is made of the Couvelaire uteroplacental apoplexy.

The relative mildness of Dr. Miller's complications may be ascribed to a high order of prenatal care in Hartford, for 98.8 per cent of all parturients in 1938 were attended by physicians, and 98.4 per cent of such patients were confined in four hospitals. In the same year the Hartford Hospital housed 54 per cent of all the city births. Ablatio occurred 79 times in private, and 41 times in ward patients, which reverses the figures for relative frequency supplied by most authorities. Hartford is a commercial city with a notable absence of a large population domiciled in tenement and slums, which may account for the differences from the type of patients seen in large municipal hospitals of maritime or manufacturing cities.

Dr. Miller's tabulation of the cases of uterine apoplexy has put my mind in a quandary, for, so far as I am aware, every authority has maintained that apoplexy was invariable evidence of a Couvelaire type of separation. The enthusiasts for cesarean section have indeed defended the operation on the score that by this means alone a diagnosis of a true uteroplacental apoplexy might be made. In Dr. Miller's report of 59 sections 57 had notations regarding apoplexy, and this condition was noted in 28 cases as being present, only 9 of which were of toxic origin. Dr. Miller states, "It is not yet clear why the separation of the placenta . . . should cause hemorrhagic infiltration which is invariably confined to the outer, and not the inner, layers of the uterus." It may be conceived that trauma might produce such ecchymotic spots, but so far as I am aware this does not hold true of toxic apoplexies. All layers are involved, especially in the site of the placental attachment. It is the extravasation of blood in the serotina which inaugurates separation and the placental cotyledons participate in this hemorrhagic infiltration.

The elimination of eclampsia as an indication for section has probably contributed more to the lessening of the mortality of the disease and of the section than all the improved therapy of the one, and the bettered technique of the other. There is a peculiar analogy between eclampsia and ablatio, and specifically for the toxic

type. Eclampsia and toxic ablatio have poisons bathing maternal and fetal tissues, great nervous depression and coma, destruction of nephritic and hepatic tissue with an arrest of function. As a result of their similarity it is as illogical to perform cesarean sections for ablatio as for eclampsia. It is needless to state contributory indications may make a section imperative.

There is a clear trend of the world's experts to limit, even to discard, cesarean section for all types of placental separation. The experience of the Rotunda Hospital, and of Irving is indicative of this trend. As late as 1939 the French Obstetrical Congress devoted a lengthy session to the consideration of placental separation. In 1,000 cases they reported the mortality following sections was 19 per cent, and for the conservative vaginal handling it was 6 per cent. Furthermore, in no sense is hysterectomy an essential part of the management, although special circumstances may require it.

So far as we know there is nothing in the physiology or anatomy of the normally implanted placenta which would lead to a toxic or nontoxic premature separation, and prevent an associated separation in placenta previa. The prompt escape of the blood in placenta previa prevents uterine distention from retained blood. The relative absence of case reports of toxic apoplexy with placenta previa must be ascribed to a lack of observation.

DR. RAYMOND E. WATKINS, PORTLAND, ORE.—During the ten-year period from 1931 to 1941, there have been 9,051 deliveries of pregnant women in the Obstetric Clinic of the University of Oregon Medical School. All were indigent patients. Premature separation of the placenta was diagnosed clinically in 30 instances. All gestations were twenty-eight weeks or more. In 24, premature separation was proved by pathologic examination, making a true incidence of one to 377. Of the remaining 6, three showed no evidence of separation on examination of the placenta, and in 3 others the placenta unfortunately was not described. All 6 patients had had typical symptoms and findings previous to delivery.

We divided our cases according to the degree of severity into (a) mild, 2; (b) moderate, 14; and (c) severe, 8.

There was a noticeable lack of prenatal supervision in these patients, 9 having none before admission to the hospital, and 10 inadequate care. Fifteen of our 24 patients showed an absence of the fetal heart beat upon admission to the hospital after symptoms of placental separation had occurred, making live birth possible in but 38 per cent.

The bleeding occurred vaginally in 21, but in 3 it was concealed. Only one with concealed hemorrhage was considered a severe case and a low cervical section was performed in this instance.

The degree of separation was partial in 21 and complete in 3. Fourteen patients entered the hospital in active labor. Twenty-one were delivered vaginally while 3 required cesarean section. The low cervical operation was performed in each instance.

The summary of our treatment is as follows: (1) Twenty-one treated expectantly; (2) membranes ruptured 8 times as a method of controlling bleeding and to induce labor; (3) forceps used in 3 patients; (4) blood transfusions in 6 patients; (5) low cervical sections in 3 severe cases; (6) manual dilatation of the cervix was not done, nor were bags used to dilate the cervix in any case.

Our maternal mortality, 4.1 per cent, consisted of one patient, who was delivered vaginally. She was a para ii who suddenly began to hemorrhage three hours after delivery with complete placental separation and died while the uterus was being packed. In retrospect we think this patient might have been saved had the uterus been packed immediately following delivery.

Eight, or 33⅓ per cent, of our 24 babies were born alive, but one premature baby died thirty-six hours after birth.

The management of patients with premature separation of the placenta has been a much disputed subject. There are those who advocate active interference early, in an effort to save both mother and child, and others who treat all patients conservatively. Both claim equally good results. Certainly no criticism could be made of the maternal and fetal mortality in the large series of cases Dr. Miller has presented, for his results are remarkable, both as to fetal and maternal survivals.

In our own experience we have not thought it advisable to do so many cesarean sections. The chance of error in early diagnosis is not inconsiderable. In 3, or 11 per cent, of our patients, the clinical diagnosis was not substantiated on examination of the placenta. The early death of the fetus is also worthy of comment in this connection. Should the woman with slight or moderate premature separation who has a dead baby be subjected to section, if by conservative measures such as artificial rupture of the membranes, the hemorrhage can be controlled? Prompt transfusions will restore her blood loss. If no further hemorrhage occurs, this method seems to us the logical one to follow.

There is a high percentage of toxemia found in every group studied. Such patients do not tolerate major surgery well. With added blood loss their risk is undoubtedly increased. The severe separation may force our hand to do a section, but, for the mild or moderate case, it has been our policy to treat the patient conservatively, delivering vaginally if possible.

Regardless of the method of delivery used the resistance of the patient must be brought to the highest level, by the arrest of hemorrhage, repeated transfusions, and other supportive treatment. Each patient presents an individual problem, and the method of management must be determined in each case by the degree of separation and the condition of the patient. No hard and fast rule can be established.

DR. JAMES R. McCORD, ATLANTA, GA.—I would like to present 92 cases of separation of the placenta, all of which were delivered from below and the great majority of them spontaneously. The total mortality was approximately 6.5 per cent.

In my opinion, in evaluating mortality in premature separation of the placenta, the condition should be divided into three groups, mild, moderate, and severe, and each group discussed separately. I do feel very strongly, and more so as the years go by, that a severe separation of the placenta is not only not an indication for a cesarean section, but is an indication for conservative treatment.

Tables I and II show our results.

TABLE I. ABRUPTIO PLACENTAE, 92 CASES

	MILD	MODERATE	SEVERE
Number of cases	46	30	16
Multiparas	71	80	87.5
Hypertension	41	66	62.5
Albumin	38	50	53
External hemorrhage	98	80	81
Shock	4.3	36	100
Rigidity	78.5	96	100
Spontaneous delivery	96	90	93
Fetal loss	54.3	76	93
Mortality	0	6.6	31

TABLE II

CAUSES OF DEATH		OPERATIONS	
Eclampsia	2	Low forceps	3
Lobar pneumonia	1	Version and extraction	3
Uremia	1	2 Shoulder presentations	
Cardiac decompensation	1	1 Transverse presentation	

DR. RUDOLPH A. BARTHOLOMEW, ATLANTA, GA.—Several decades ago, it came to be realized that the employment of forcible measures of delivery, such as internal version and extraction, manual dilatation of the cervix, difficult forceps delivery or cesarean section, was a large factor in the high mortality of eclampsia. Substitution of supportive measures, induction of labor, and a minimum of trauma effected a reduction in mortality from the figures of 15 to 20 per cent to 5 to 7 per cent. We are coming to the same viewpoint in regard to separation of the placenta.

Eclampsia and separation of the normally implanted placenta are fundamentally of the same nature. The latter is preceded by typical manifestations of toxemia in the majority of cases, and the pathology in the placenta is identical with that of eclampsia. However, in separation of the placenta, we are confronted with two complications: hemorrhage and a marked tendency to shock, the latter being particularly dangerous.

I believe that the employment of conservative treatment is most important. By that I mean when the patient is first seen, dismiss the idea of delivering her, but rather give supportive treatment with glucose solution, whole blood or plasma intravenously, along with sedatives. Following improvement in her condition, rupture the membranes, apply an abdominal binder if necessary, and await within reason a spontaneous delivery. This will obtain much better results than if we rush in immediately with operative procedures. I think the impression should go out, particularly to the average man, that this is a condition which he can treat with greater success by conservative methods regardless of surroundings.

This is a case of separation of the placenta. You see the dark areas of acute infarction scattered through the whole strip identical in every way with those seen in eclampsia. The consistency and similarity of the placental findings in each condition have been such as to make me realize that cases of separation of the placenta are practically all on a toxic basis and that the cases due to trauma are negligible.

DR. MILLER (closing).—If our experience has served anything, it is to show that where one is confronted with a severe ablatio and what you would all recognize as an absolute indication for cesarean section, you can still do a cesarean safely if you pay attention to the fundamentals of blood loss replacement and anesthesia. Our experience has not met with the forebodings of those who have threatened us with dire consequences.

We had one death three weeks ago, since this series ended. That patient had had a systolic blood pressure of over 200 for more than three years and died with massive cerebral hemorrhage two hours after the cesarean section was done under block anesthesia, with a substitution of 1,000 c.c. of citrated blood. Personally, I should not have done a cesarean section in this case, though I believe that the operation had little to do with her death.

PELVIC PAIN*

A Follow-Up Study

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IN ASSEMBLING data for a previous paper[15] on pelvic pain it was found that approximately one-sixth of the women who consulted physicians at the Mayo Clinic in 1936 had ailments concerned with pain in the region of the pelvis. For that study, the records of 500 of these women were analyzed and data were obtained on each patient's age and civil state, on the site and frequency of the pain, and on the physical findings and diagnosis. In this present paper the subject of pelvic pain is reviewed briefly. Then the results are given of a study concerning relief of pelvic pain following treatment. Included in the study were those of the 500 patients who were living four years or more after the time of the previous study and concerning whom information could be obtained.

PELVIC PAIN

Illustrations of the nervous system commonly found in textbooks may fail to show the continuity that exists between the innervation of the pelvic viscera and that of the abdominal viscera and the somatic structures.[1, 6, 7, 12] Fig. 1 illustrates the anatomic distribution of the somatic and autonomic (sympathetic and parasympathetic) nerve fibers which are of concern to the gynecologist. It is to be noted that the autonomic nervous structures form a closely integrated system of nerve fibers; that the sympathetic chain supplies fibers for all the abdominal viscera and that there are numerous levels at which impulses can leave or enter the sympathetic chain and the central nervous system. The human body is an integrated whole and nerve fibers pass to and come from viscera such as the stomach, colon, and pancreas, as well as from the uterus and its adnexa.

The so-called sympatheticosensory fibers are the fibers which carry pain impulses from the pelvic viscera and are, therefore, most important to this discussion.[5, 18] In a strict physiologic and pharmacologic sense, these fibers have nothing in common with the true sympathetic nervous system. They are simply sensory fibers which have their cell stations in the posterior root ganglia and differ in no way from somatic sensory fibers except that they pass to the spinal cord through the anatomic sympathetic system. Properly they should be termed viscerosensory fibers.

With the foregoing facts in mind, it is less unexpected than otherwise to learn that Lewis and Kellgren, by injecting saline solution into the

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interspinous ligaments, were able to produce syndromes typical of anginal and renal colic. Because of these findings they stated that "all the chief subjective phenomena usually associated with visceral disease

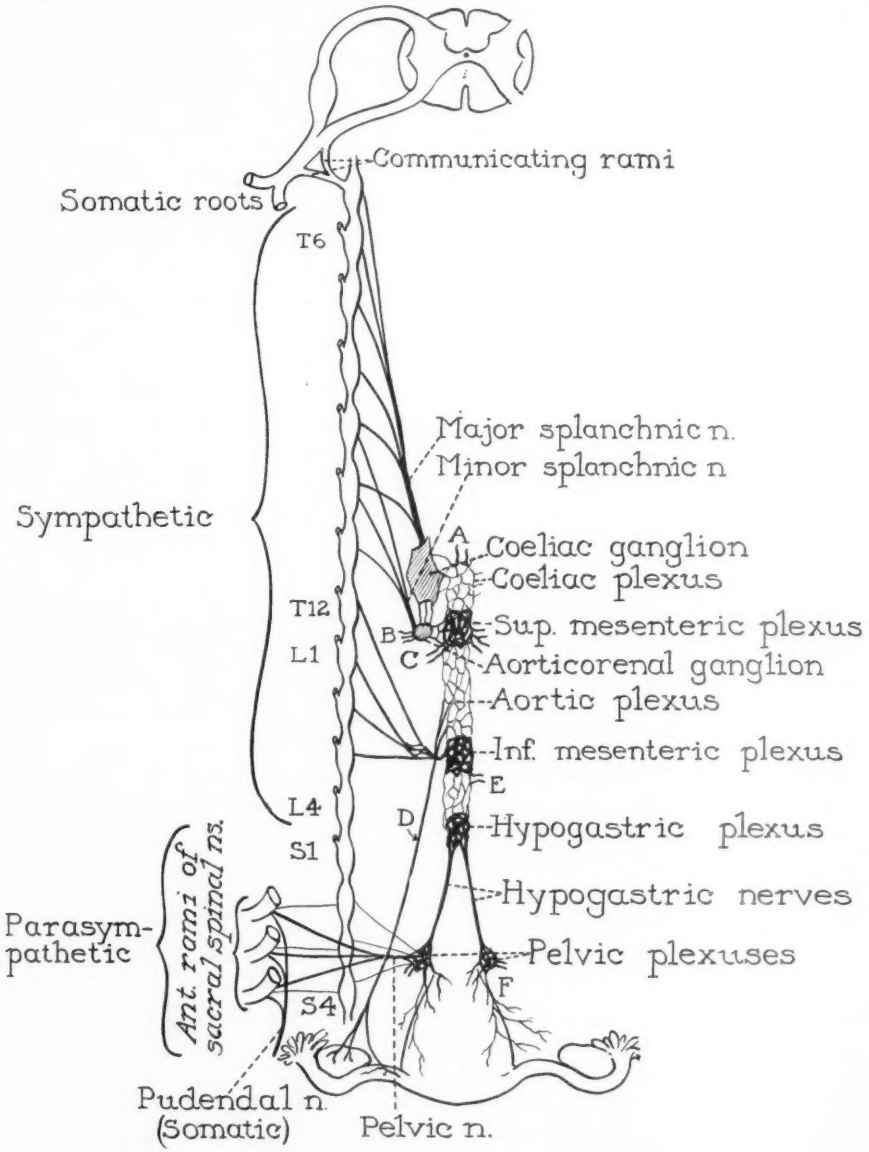

Fig. 1.—Anatomic distribution of the somatic and autonomic nerve fibers of concern to the gynecologist. *A*, Fibers to esophagus, stomach, duodenum, pancreas, liver, gall bladder and spleen; *B*, to kidney; *C*, to small intestine, cecum, ascending and transverse colon; *D*, to ovary and Fallopian tube; *E*, to sigmoid and descending colon; *F*, to rectum, bladder, and uterus. Somatic roots supply abdominal wall and parietal peritoneum. Pudendal nerve supplies perineal structures.

can be reproduced through purely somatic channels, [which] is opposed to the concept that somatic and visceral pain are to be regarded as separate entities." These authors concluded that, "the pain of visceral and

somatic disease is derived from the direct stimulation of a common system of nerves, which supply all the deep lying somatic tissues concerned and by way of the anatomical sympathetic, also supply a limited amount of the tissues contained within the visceral peritoneum; and . . . these painful impulses are either identical with, or are generally associated with the afferent impulses which set up reflexly a common series of motor and sensory reactions.'' This statement is contrary to the older hypotheses of Lennander, Ross, Mackenzie,[10, 11] Head and Morley,[13, 14] but it would seem factual.

In the evaluation of pain in general it is well to remember that some of the different sensations are attributable to stimulation of special, differentiated end-organs of nerves, such as encapsulated[17] end-bulbs for touch, or the Meissner corpuscles for touch and pressure. However, sensations of pain occur, owing to stimulation of free, undifferentiated nerve fibers. As the visceral supply of such nerve fibers is sparse, and because nerve fibers and cells which supply the viscera are much smaller than those which supply somatic structures, it is not difficult to understand the difference in the efficiency of sensations of pain when the viscerosensory and somaticosensory systems are compared. Because of this difference it must be true that viscera are insensitive to stimuli unless such stimuli are massive and that localization of visceral pain is somewhat vague.

It has been shown[9] that the viscera are insensitive to ordinary stimuli such as burning and crushing but are sensitive to such stimuli as an increase in tension. Tension in the tissues may be caused by inflammation, edema, or vascular engorgement. It is an obvious but seldom appreciated fact that inflammation can exist without causing pain. In other words, there are painful and painless types of inflammation. Kinsella[3, 4] has well illustrated this by recalling that an acutely inflamed appendix is painful because the appendix is hard and under tension but an acute gastric ulcer is not painful until induration and tension occur. A striking example is the disappearance of pain after incision of an abscess; the inflammation is there both before and after incision but the pain disappears with the decrease in tension.

Another important physiologic concept is that sensory impulses received in the posterior horns are integrated at the level where they are received; they may be inhibited or relayed.[19] As far as the somatic sensory apparatus is concerned it is unlikely that, under ordinary circumstances, the end-organs of the discriminative senses (touch temperature and so on) could be stimulated without, at the same time, the pain receptors being stimulated. Yet the sensations of the discriminative senses reach the level of consciousness while those of pain may not, because of being inhibited in the posterior horns of the spinal cord. It would seem that this same finding applies to impulses which are received from the viscera. This is of particular clinical importance, because this inhibition of painful impulses may be weakened by worry, chronic exhaustion, or general ill health. Under such circumstances potential pain stimuli, which ordinarily would be unnoticed, reach the consciousness of the individual with abnormal ease. It is likely that this is the explana-

tion of many of the pains and discomforts suffered by patients who reveal clinical evidence of chronic nervous exhaustion or constitutional inadequacy. These patients are so worn by their cares or exhaustion that the minimal impulses received from the viscera are not inhibited at the customary level in the spinal cord; consequently they are suffering, more or less constantly, from some pain or discomfort.

THE FOLLOW-UP STUDY

This follow-up study of pelvic pain was attempted with the full realization that pain is not a diagnostic entity and that treatment or operation is ordinarily carried out for the relief or cure of a pathologic condition rather than primarily for the relief of any one symptom, such as pain. However, it seemed to be desirable to know the percentage probability of relief of pain associated with various pelvic disorders.

At the risk of repetition of some material included in the opening paragraph, it should be said here that four or more years following examination of them in 1936, questionnaires were sent to the 500 patients included in the previous study.

Each patient was asked whether the pain was completely relieved, partly relieved, or not relieved. If the patient was not treated or operated upon at the clinic she was asked concerning whatever subsequent treatment or operation she may have undergone. Replies were received to 310 of the 500 questionnaires or 62 per cent. Twenty-three patients had died during the interval of four years and were excluded from the study. Therefore, the statistics are based on 310 patients.

TABLE I. CONDITION RELATIVE TO PAIN OF ALL PATIENTS AND OF PATIENTS WHO MADE CERTAIN COMPLAINTS

PAIN, AS REPORTED ON FOLLOW-UP	TOTAL PATIENTS FOLLOWED		PATIENTS WHOSE COMPLAINT ON FOLLOW-UP WAS OF:							
			LOWER ABDOMINAL PAIN		BACKACHE		MENSTRUAL PAIN		MULTIPLE COMPLAINTS	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Complete relief	131	43	91	47	14	26	13	45	13	38
Partial relief	91	29	50	26	23	43	9	31	9	27
Same as, or worse than, 4 years before	88	28	52	27	17	31	7	24	12	35
Total	310	100	193	100	54	100	29	100	34	100

RESULTS IN GENERAL

The over-all results are represented in Table I. This tabulation was made without regard to the original diagnosis or to the type of treatment which was employed. To simplify the tabulation further, all patients who had lower abdominal pain were grouped together, as were those who had backache, or dysmenorrhea, or multiple causes of complaint. Of the 310 patients, 193, or almost 62.3 per cent, complained primarily of lower abdominal pain. The remaining 37.7 per cent complained of backache or menstrual pain, or they made multiple complaints. The general statement can be made that, regardless of situation of their original pain, nearly three of every ten patients had not obtained relief.

TREATMENT AND ITS RESULTS

In general, the treatment of pelvic pain conformed to accepted conservative standards. For example, pelvic inflammatory disease was treated usually by the use of pelvic heat and, less commonly, by surgical measures; chemotherapy was not employed to any great extent in 1936. According to indications, neoplasms were treated surgically or by radium and roentgen therapy. The management of patients with nervous exhaustion, constitutional inadequacy, or functional disorders was often most difficult. Painstaking physical and laboratory examination made the diagnosis more certain and sympathetic attention to the patient's complaints was valuable in gaining her confidence. Such confidence placed in the physician enabled him to reassure the patient and to develop a constructive program for regaining nervous stability, without which such pain was not relieved.

No attempt was made to tabulate the exact treatment which the patients had received. As a form of treatment, however, surgery occupies an important place in the management of conditions associated with pelvic pain. Aside from necessary operative skill, the success of surgical measures is necessarily dependent on the acuity of the physician in determining whether a given operation should be performed. Ordinarily, pelvic surgical operation is performed to remove diseased tissue, or as a restorative plastic procedure, and is seldom employed primarily for relief of pain. A notable exception is presacral neurectomy which may be employed in cases of intractable dysmenorrhea. It is, of course, important to relieve pain and the statistics given in Table II reveal that

TABLE II. EFFECT OF SURGICAL PROCEDURES ON PAIN OF PATIENTS WHO MADE CERTAIN COMPLAINTS

COMPLAINT ON FOLLOW-UP	TOTAL PATIENTS FOLLOWED	PATIENTS SUBJECTED TO SURGICAL OPERATION							
		NUMBER	PAIN, AS REPORTED ON FOLLOW-UP						
			COMPLETE RELIEF		PARTIAL RELIEF		SAME AS, OR WORSE THAN, 4 YEARS BEFORE		
			NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	
Lower abdominal pain	193	99	58	59	19	19	22	22	
Backache	54	6	4	66	1	17	1	17	
Menstrual pain	29	14	8	57	4	29	2	14	
Multiple complaints	34	12	7	58	3	25	2	17	
Total	310	131	77	58	27	21	27	21	

this was accomplished with reasonable frequency. Almost half of the patients studied underwent some surgical procedure. Comparatively few patients with backache, however, were subjected to surgical operation. This is a reversal, now generally accepted, of the formerly prevalent opinion that backache is almost always a symptom of pelvic disease. Because of its relative infrequency, probably surgical operations performed on patients who complained of backache should be ignored in this discussion. Omitting those with backache, therefore, it is evident

that about 6 of 10 patients were entirely relieved of pain by surgical measures, the pain of 2 of 10 was improved, and that of another 2 of 10 was the same as four years before or worse.

TABLE III. EFFECT ON PAIN OF SURGICAL TREATMENT COMPARED WITH THAT OF NONSURGICAL TREATMENT

PAIN AS REPORTED ON FOLLOW-UP	PATIENTS TREATED AND FOLLOWED			
	SURGICALLY		NON-SURGICALLY	
	NO.	%	NO.	%
Complete relief	77	58	54	30
Partial relief	27	21	64	36
Same as, or worse than, 4 years before	27	21	61	34
Total	131*	100	179†	100

*Eleven patients excluded; died in the interval of four years.
†Twelve patients excluded; died in the interval of four years.

In Table III comparison is made, on the basis of relief of pain, between patients subjected to surgical treatment and those subjected to medical treatment. Evidently, of patients treated surgically, a larger percentage (79 per cent) were completely or partly relieved than was true of those

TABLE IV. EFFECT ON PAIN REPORTED BY PATIENTS WHO HAD RECEIVED CERTAIN DIAGNOSES

DIAGNOSIS	TOTAL ORIGINAL DIAGNOSES*	PAIN AS REPORTED ON FOLLOW-UP					
		COMPLETE RELIEF		PARTIAL RELIEF		SAME AS, OR WORSE THAN, 4 YEARS BEFORE	
		NO. (DIAGNOSES)	% (DIAGNOSES)	NO. (DIAGNOSES)	% (DIAGNOSES)	NO. (DIAGNOSES)	% (DIAGNOSES)
Chronic nervous exhaustion	55	14	25	17	31	24	44
Pelvic inflammatory disease	29	13	45	10	34	6	21
Lumbar or sacral pathologic condition	53	10	19	23	43	20	38
Appendicitis	31	19	61	7	23	5	16
Ovarian cysts	12	7	58	4	33	1	9
Uterine myomas	36	18	50	6	17	12	33
Dysmenorrhea	30	13	43	9	30	8	27
Constipation	25	8	32	8	32	9	36
Retroversion	18	4	22	6	33	8	45
Cervicitis	18	12	67	1	5	5	28
Relaxation†	17	8	47	5	29	4	24
Carcinoma	4‡	3	75	0	0	1	25
Endometriosis	9	5	56	3	33	1	11
Indeterminate	16	5	31	5	31	6	38
All others	54	24	44	12	22	18	34
Total diagnoses	207	163	40	116	29	128	31
Actual number of patients	310						

*Some patients received more than one diagnosis.
†Relaxation of structures supporting pelvic viscera.
‡Ten of the original 16 patients with carcinoma had died in the interval of four years.

treated medically (66 per cent). The greater efficacy of surgical measures is understandable because such measures are chosen in those definite conditions in which it is almost always possible to remove or correct the condition which is causing the pain. Nonsurgical treatment, on the other hand, must necessarily be employed in a larger percentage of instances wherein the diagnosis is indeterminate or the cause of the pain is functional rather than organic.

RELIEF OF PAIN IN RELATION TO DIAGNOSIS

It was obviously impossible to tabulate each of the many diagnoses; nevertheless Table IV is concerned with relief of pain according to some of the various diagnoses. As might be anticipated, a survey of this table shows that those patients who were nervously exhausted obtained the least benefit; nearly half of them stated that their pain was the same as it had been four years before, or worse. The observation that carcinoma almost never causes pain until it is in an advanced stage is supported by the known death of 10 of the original 16 patients with carcinoma in the interval of four years; 3 of the 4 known survivors stated that they had no pain.

SUMMARY AND CONCLUSIONS

Pain from the pelvic viscera reaches the consciousness of the individual through somatic afferent nerve fibers, called the "viscerosensory nerves," which pass upward from the pelvic viscera in the sympathetic chains; these nerves pass into cell stations at their proper level in the spinal cord where the stimuli are integrated or sorted out. The meager number and size of viscerosensory nerves, no doubt, account for the vagueness of localization of pain by the average individual unless the lesion affects also the parietal peritoneum which is more richly supplied by somatic nerves. When the normal selective function of the cell stations in the cord is weakened by vitiating disease or nervous exhaustion, many stimuli which would ordinarily be submerged reach the consciousness of the individual as pain.

When a reasonably accurate diagnosis is made of pelvic lesions which cause pain and which are amenable to surgical measures complete or partial relief of pain may be expected in 79 per cent of cases, depending on the condition and the nature of the operation.

Nonsurgical lesions or pain for which organic cause is not found, may be relieved in not more than 66 per cent of cases; in this group fall a considerable number of patients, about a fourth of all patients who complain of pelvic pain, who have no demonstrable organic lesion or who suffer from varying degrees of chronic nervous exhaustion. The scientific integrity of the physician is best maintained by his explaining to this type of patient, who is difficult to satisfy and reassure the physiologic basis of her pain.

REFERENCES

(1) *Davis, A. A.:* Brit. M. J. 2: 1, 1934. (2) *Head, Henry:* Brain 16: 1, 1893. (3) *Kinsella, V. J.:* Brit. J. Surg. 27: 449, 1940. (4) *Kinsella, V. J.:* M. J. Australia 1: 681, 1940. (5) *Kuntz, Albert:* The Autonomic Nervous System, Philadelphia, 1929, Lea & Febiger, pp. 399-431. (6) *Labate, J. S., and Reynolds, S. R. M.:*

AM. J. OBST. & GYNEC. 34: 1, 1937. (7) *Learmonth, J. R.:* Brain 54: 147, 1931. (8) *Lennander, K. G.:* Observations on the Sensibility of the Abdominal Cavity (translated by A. E. Baker), London, 1903, J. Bale, Sons & Danielsson. (9) Lewis, *T., and Kellgren, J. H.:* Clin. Sc. 4: 47, 1939. (10) *Mackenzie, James:* Brain 16: 321, 1893. (11) *Mackenzie, James:* Symptoms and Their Interpretations, ed. 3, London, 1918, Shaw & Sons. (12) *Meigs, J. V.:* New England J. Med. 222: 187, 1940. (13) *Morley, John:* Abdominal Pain, New York, 1931, William Wood & Company. (14) *Morley, John:* Brit. M. J. 2: 1270, 1937. (15) *Mussey, R. D.:* AM. J. OBST. & GYNEC. 37: 729, 1939. (16) *Ross, James:* Brain 10: 333, 1888. (17) *Spiegel, E.:* Internat. Clin. 3: 140, 1938. (18) *White, J. C.:* The Autonomic Nervous System; Anatomy, Physiology, and Surgical Treatment, New York, 1935, The Macmillan Company, pp. 102-114. (19) *Wright, Sampson:* Applied Physiology, ed. 7, New York, 1940, Oxford University Press, pp. 33-50 and 171-239.

DISCUSSION

DR. HOUSTON S. EVERETT, BALTIMORE, MD.—I shall pass over Dr. Mussey's treatment of the neurologic and physiologic causes of pain and shall confine my discussion to emphasizing a few points brought out in his clinical analyses. In the first place, it should be noted that in his table of diagnoses there are found to be 74.4 per cent of his patients who were suffering from gynecologic conditions which might have contributed to their pain, but there were 81.6 per cent in whom some possible cause other than a gynecologic one was found. The multiplicity of conditions occurring in many patients, as he has mentioned, accounts for the fact that these two figures add to more than 100 per cent. Dr. Mussey as a gynecologist is distinctly to be congratulated on finding a greater number of nongynecologic than gynecologic conditions. I am afraid that the surgical specialist in any field is often too prone to attribute a patient's symptoms to those organs with which his line of work is particularly concerned.

Another point that is worthy of emphasis is the appreciable percentage of patients (17.6 per cent) in whom he found the pain due to chronic nervous exhaustion. This group of patients, as his results have shown, always constitute the most difficult therapeutic problem so far as relief of pain is concerned. We may divide patients suffering from pelvic pain into three large groups: First, those who have easily demonstrable organic lesions which require surgical correction and in whom the pain seems to be definitely associated with these lesions and is usually relieved by their correction. On the opposite end of the scale we may place those patients in whom, after very careful studies, no definite organic lesions can be demonstrated. Most of these patients should probably be placed in the group referred to under various names, such as chronic nervous exhaustion, as used by Dr. Mussey, or functional psychoneurosis with tension state, as is more frequently used by the psychiatrists with whom I am familiar. In the first of these groups the outlook for the relief of pain is excellent. In the second it is very poor and in the experience of most of us, I believe, these patients are usually best treated by thorough diagnostic study so that they can be positively assured of the absence of organic disease, after which some type of psychiatric regime should be instituted. It is common experience that manipulative treatments, such as unnecessary surgery or cystoscopic treatments, are likely to have a harmful rather than a beneficial effect on such patients.

Probably the most difficult group of all is that in which the patients have some organic lesion which at first seems that it might account for the pain, but the correction of which fails to give relief. A later analysis of many of the members of this group will show that they should originally have been placed in the group of psychoneuroses, and treatment along these lines eventually has to be instituted before any success is achieved.

I was a bit disappointed at the failure to find in Dr. Mussey's table of diagnoses any mention of disease of the urinary tract. Many urologists dealing particularly with the female, to mention only Hunner and William E. Stevens as outstanding examples, have given much emphasis, perhaps undue emphasis, to the urinary tract as a contributory factor in many types of pelvic and other pain. Even though their emphasis may be somewhat exaggerated an examination of the urinary tract should certainly not be omitted in the search for the cause of pain in a patient in whom it seems obscure. From my own experience, I am quite positive that no group of

500 women suffering from pelvic pain could be found in which there would not be discovered a substantial number of urinary tract lesions if they were looked for.

In order to determine the possible effect on the urinary tract of various gynecologic conditions one of my associates and I recently have made complete urologic studies on a series of 100 patients. We found varying degrees of dilatation of the ureters and pelves in 50 per cent of these. After appropriate treatment of their gynecologic conditions about 30 of the 50 patients who originally showed dilatation have been subjected to restudy. In about half of these the urinary tracts had failed to return to normal although in some instances, a number of months had elapsed since the completion of their gynecologic treatment. It occurred to me that this finding might throw some light upon the occasional failure completely to relieve pain by the appropriate surgical correction of some gynecologic lesions.*[15]

DR. MUSSEY (Closing).—I am glad that Dr. Everett emphasized the group of patients with pelvic pain who have organic trouble and also psychoneurosis. Observation of women with pelvic pain has demonstrated that one must be guarded in promising complete relief of complaints, and particularly of pain, to patients who have conditions which require operation. In reference to lesions of the urinary tract, I may say that these were included under the heading "multiple complaints."

*Percentages given in this discussion are based on the following article: *Mussey, R. D.:* AM. J. OBST. & GYNEC. 37: 729, 1939.

A CRITICAL ANALYSIS OF BLOOD LOSS IN 2,000 OBSTETRIC CASES*

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During the past ten years it has been agreed[1, 2, 4, 6-8, 11-16, 18] that the factors which contribute to increased blood loss are: increase in the weight of the mother, of the baby, and of the placenta, increased length of labor, general anesthesia, forceps delivery, laceration of perineum or episiotomy and last, mismanagement of the third stage.

The incidence of post-partum hemorrhage is given variously from 0.74 per cent (Smith[3]) to Peckham's figure[4] of 6.14 per cent and Pastore's[10] figure of 6.4 per cent, and the basic volume is expressed as from 500 to 600 c.c. or as Pastore[11] argues over 1 per cent of maternal body weight. Dieckmann and Daily[7] consider forceps delivery with episiotomy adds 235 c.c. to the volume lost through spontaneous delivery, while Calkins says episiotomy adds 60 c.c., a large baby adds 100 c.c., and mismanagement of the third stage adds 200 to 400 c.c. to the average blood loss.

The Dickinson-Pomeroy technique of third stage management is advocated by Smith[3] and Brandt.[5] Pastore and Stander[16] recommend the use of Calkins' principle of recognition of placental separation and advise the Pastore modification of the method of expression whereby the placenta is not used as a piston but is kept up out of the pelvis.

The routine injection of pituitrin intramuscularly is advocated by many men either before or after the placenta is delivered. Doerr[9] advises its use intravenously as do Dorset[13] and Peckham.[4] Many others employ the newer ergonovine intramuscularly (Smith[17]) or, as Davis[18] avers, intravenously even at the onset of the third stage.

Most men agree that, if necessary, manual removal of the placenta should be performed and the uterine cavity packed although Cosgrove[19] is definitely opposed to this latter procedure.

The blood loss should be replaced by glucose saline intravenously and (or) transfusion of blood. This, says Pastore,[10] will tend to minimize puerperal infection and decrease hospital stay.

For some time we have been amazed to note a greater measured blood loss following delivery than we had judged there would be. With this in mind we feel that a review of a series of consecutive deliveries would be justified since it would enable us to determine the average blood loss, the incidence of post-partum hemorrhage (i.e. 600 c.c. or more), the factors which contribute to the increase, the causes, and prophylactic measures to prevent this grave complication. That increased blood loss is a grave complication is proved by the records of the Province of Alberta for the years 1936 to 1939, inclusive. Dur-

*Read, by invitation, at the Sixty-Sixth Annual Meeting of the American Gynecological Society, Colorado Springs, Colo., May 26 to 28, 1941.

ing this period, 64,607 deliveries were recorded. In this group there were 161 maternal deaths, and of this number, 49, or 30 per cent, were considered due to post-partum hemorrhage, a figure which surpasses Cosgrove's[19] recorded incidence of 25 per cent. No records are available of the number of mothers whose puerperium has been prolonged or who have become chronic invalids directly or indirectly as a result of excessive blood loss, which has been recognized too late, or not at all, by the attending physician. And indeed he is unlikely to appreciate the significance of excessive blood loss during the third stage unless he is keenly interested and has a simple but relatively accurate method of measurement.

There are very few hospitals in Canada where any attempt is made to measure blood loss. Some, it is true, try to estimate the volume, but it is obvious that this is markedly inaccurate and, indeed, sometimes misleading. Sad to relate, a few make no attempt at even an estimation. Since we cannot find any published record from any Canadian hospital obstetric service, it is hoped that this review will stimulate interest and provide the impetus for further investigation of this problem throughout the Dominion.

Our apparatus for measuring blood loss is cheaply made, easily attached to any table and is relatively accurate. Amniotic fluid which collects following rupture of the membranes can be easily dumped, and the amount of "after waters" in the pan usually balances the amount of blood which collects on the linen.

Our series comprises 2,000 consecutive vaginal deliveries up to Dec. 31, 1940, of which 800 were primigravidas, and 1,200 were multigravidas. We have made no attempt to classify them further. The average blood loss for all primiparas was 388 c.c., for multiparas it was 280 c.c., and for the series averaged 323 c.c. As before stated, this is higher than we expected.

TABLE I. WEIGHT OF PATIENT AND BLOOD LOSS

WEIGHT (POUNDS)	PRIMIPARA		MULTIPARA		TOTAL		P.P. HEMORRHAGE	
	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS
Under 120	20	266	17	321	37	291	2	775
121-140	247	382	359	278	607	320	94	840
141-160	391	384	436	263	927	314	140	785
161-180	111	405	213	310	324	343	58	912
181-200	25	482	49	255	74	332	12	899
Over 201	5	516	26	403	31	421	8	886
	800		1,200		2,000		314	

Table I shows the relation between weight of the patient and blood loss. It is evident that the increase in average blood loss corresponds to the increase in the mother's weight. This same tendency is also apparent in the group whose blood loss is 600 c.c. or more. In Table II there is a similar increase following the delivery of a large baby or of twins.

In Table III the same holds true; in the main the increased weight of the placenta is more likely to result in increased blood loss, although in approximately 75 per cent of the cases, the placental weight aver-

TABLE II. WEIGHT OF BABY AND BLOOD LOSS

WT. IN GRAMS	PRIMIPARA		MULTIPARA		TOTAL		P.P. HEMORRHAGE	
	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS
Under 2,500	46	283	60	158	106	221	10	720
2,500-2,999	136	304	184	234	320	264	29	775
3,000-3,499	370	375	463	246	833	303	117	813
3,500-4,000	197	475	351	303	548	365	110	848
Over 4,000	39	469	127	383	166	403	41	897
Twins	12	562	15	502	27	529	7	997
	800		1,200		2,000		314	

TABLE III. WEIGHT OF PLACENTA AND BLOOD LOSS

WT. IN GRAMS	PRIMIPARA		MULTIPARA		TOTAL		P.P. HEMORRHAGE	
	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS
Under 453	36	278	44	245	80	260	6	757
454-567	346	358	476	251	822	296	111	812
568-680	266	397	394	274	660	323	97	847
681-793	101	465	178	325	279	375	63	815
794-907	27	403	65	341	92	359	17	835
908-1,134	21	577	34	426	55	484	17	957
Over 1,134	3	400	9	397	12	399	3	870
	800		1,200		2,000		314	

ages between 453 Gm. and 680 Gm. The smaller blood loss where the placenta weighed over 1,134 grams is probably not consistent with that which would accrue in a large number of such cases. This, as others have pointed out, suggests that the amount of blood loss is proportionate to the amount of retraction of the uterus which is necessary following delivery.

TABLE IV. DURATION OF LABOR AND BLOOD LOSS

DURATION	PRIMIPARA		MULTIPARA		TOTAL		P.P. HEMORRHAGE	
	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS
Under 3 hr.	25	231	201	259	226	256	29	770
3-10 hr.	296	377	649	285	945	314	135	840
10-20 hr.	333	371	269	290	602	335	99	806
20-30 hr.	101	475	66	264	167	391	37	868
Over 30 hr.	45	480	15	248	60	422	14	907
	800		1,200		2,000		314	

Table IV shows a progressive increase in blood loss varying directly with the duration of the labor. The average duration in primiparas was calculated as fourteen hours, that in multiparas as nine hours; the total average as 10.5 hours. The increased average in primiparas was due to several factors: almost 60 per cent were in labor more than 10.5 hours as compared to 29 per cent of the multiparas. This increased length of labor leads to an increased amount of sedation as a rule, an increase in operative delivery, and greater fatigue of the mother.

The method of delivery in its relation to blood loss is shown in Table V. Of the 2,000 cases, 66 per cent delivered spontaneously with an average blood loss of 278 c.c. With low forceps delivery (24 per cent), the average blood loss was increased 126 c.c. Midforceps delivery further increased the blood loss as might be expected. In breech de-

TABLE V. METHOD OF DELIVERY AND BLOOD LOSS

METHOD	PRIMIPARA		MULTIPARA		TOTAL		P.P. HEMORRHAGE	
	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS
Spont.	371	323	965	261	1,336	278	156	812
Low Forceps	314	429	162	356	476	404	112	828
Midforceps	19	541	8	362	27	488	7	923
Forceps Rot. Midforceps Manual Rot.	26	551	12	245	38	454	10	837
Midforceps	24	491	10	488	34	490	11	932
Breech	34	385	25	247	59	327	9	863
Twins	10	477	14	502	24	492	7	963
Inc. of Cerv.	1	1,225	0	0	1	1,225	1	1,225
Version and extraction	1	200	4	429	5	383	1	660
	800		1,200		2,000		314	

livery and version and extraction, the blood loss surprisingly was lower than in low forceps delivery. While the number of cases is smaller, yet the incidence of breech presentation (3 per cent) conforms to the accepted figure. We employ version and extraction rarely, which explains the small number of cases. It is possible a larger number would result in a relatively greater blood loss.

TABLE VI. STATE OF PERINEUM AND BLOOD LOSS

	PRIMIPARA		MULTIPARA		TOTAL		P.P. HEMORRHAGE	
	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS
Intact	65	189	564	206	629	206	39	786
Lac. 1st Deg.	71	266	300	288	371	284	44	812
Lac. 2nd Deg.	20	365	29	343	49	352	10	849
Lac. 3rd Deg.	4	425	1	550	5	450	1	600
Episiotomy	613	397	306	396	919	395	195	828
Episiotomy and side wall tear	27	980	0	0	27	980	25	1,019
	800		1,200		2,000		314	

Table VI demonstrates the increasing average blood loss where the perineum was torn or incised. In 32 per cent of all cases the perineum was intact, and the average blood loss was 206 c.c. Even a slight laceration (19 per cent) resulted in an average increase of 78 c.c. A second degree laceration resulted in a further increase of 136 c.c., while in the 5 cases wherein a third degree laceration occurred, the blood loss more than doubled that from an intact perineum. Our practice of performing episiotomy is quite evident from the table. Seventy-seven per cent of primiparas and 25 per cent of multiparas were so treated with an average blood loss of 395 c.c., an increase of 189 c.c. over the loss through the intact perineum. This increase is more than we expected, so much so, that we are considering a change or at least a modification of this procedure. In 27 cases there occurred an extension of the episiotomy upward along one or both lateral walls of the vagina. These lacerations bleed profusely, are difficult to repair, and explain the average blood loss of 980 c.c., a truly alarming amount! These accidents are not all due to inexpert forceps application, or traction, but are usually associated with a narrow pelvic outlet, a long sacrum, and

a small vagina, a combination which is relatively common in our experience, and which merits our constant attention. A just criticism might be made that we did not iron out the lower vagina and perineum, but this has happened in spite of the fact that the ironing out was done, and moreover that the perineum was infiltrated with local anesthesia. We feel that this accident cannot be avoided in a certain number of cases. Local infiltration of the perineum in our experience decreases the local blood loss and lessens the amount of general anesthesia, thereby minimizing uterine atony. It does, however, to a large extent abolish the "perineal urge" and so increases the use of outlet forceps application.

TABLE VII. DURATION OF THIRD STAGE AND BLOOD LOSS

DURATION	PRIMIPARA		MULTIPARA		TOTAL		P.P. HEMORRHAGE	
	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS
Under 6 min.	176	378	323	245	499	292	69	798
6-15 min.	466	366	757	279	1,223	312	169	828
16-30 min.	139	450	109	369	248	415	68	836
31-60 min.	14	474	10	380	24	438	6	967
Over 60 min.	5	625	1	50	6	529	2	1,112
	800		1,200		2,000		314	

The average duration of the third stage was thirteen minutes. There was, as shown in Table VII, a progressively increasing blood loss as the duration of the third stage was prolonged. This is very noticeable in that group (15 per cent) where the third stage was longer than fifteen minutes. This is due probably to atony of the uterus, to partial separation of the placenta, or to tardy recognition of complete separation. In this table, the blood loss in primiparas averaged 100 c.c. more than in multiparas, and is due most likely to the extra blood loss from a larger laceration or episiotomy. However, the conduct of the third stage does play a part in the blood loss. Early recognition of placental separation is essential whether by the criteria of Calkins, or by individual modification. We do not believe that the placenta should be expressed after the first uterine contraction, but rather that the uterus should rise in the abdomen, should become globular, firm, against the anterior abdominal wall and be freely mobile. This may need more than one contraction but is usually indicated by slight uterine bleeding. We have found Pastore's method of expressing the placenta ideal for most cases except where the abdominal wall is thick and resistant, when it then is difficult. However, if the uterus is pushed into the pelvis we believe it should be elevated immediately after the placenta is out even if combined abdominal and vaginal pressure is necessary. At this stage, early in the series, ergonovine 0.2 mg. (ergotrate, Lilly) was injected intramuscularly, but we soon found that a quicker response could be obtained by injecting the alkaloid immediately after the birth of the baby, with no greater tendency to contraction of the cervix, and incarceration of the placenta. Lately we have been injecting ergotrate intravenously as soon as the baby is born. This has speeded up placental separation markedly and to date has yielded no untoward results, although the increased possibility of contraction of the cervix with incarceration of the placenta must be recognized.

Uterine tamponade was employed in 24 instances. Where, in spite of massage and medication, we are unable to keep the uterus elevated and

well contracted, or where vaginal wall oozing persists, we do not hesitate to pack the uterine cavity. For this we use a homemade instrument, a sigmoidoscope 2 cm. in diameter whose obturator has been converted into a trident. The tube is inserted into the uterine cavity and 2 inch dry gauze is pushed through the lumen as far as desired. The packer is gradually removed and the vagina in turn is packed, 3 to 6 yards of gauze in all being used. This keeps the uterus elevated, effectively controls oozing and may be removed twelve to twenty-four hours later. In our experience there has been no relative increase in morbidity where packing has been inserted and, where all other measures seem to fail, we find it a valuable asset.

It would be ideal for every woman whose blood loss is 600 c.c. or more to have a blood transfusion immediately, but from a practical point of view, some of them do not seem to require it. The reaction to blood loss varies according to size and weight, and this must be taken into consideration. In some patients the restoration of fluid volume by intravenous glucose is sufficient—in others this must be supplemented by blood transfusion. This restoration of blood volume undoubtedly reduces morbidity and mortality during the puerperium.

A greater interest in the technique of the third stage leads to a closer observation of the mechanism and quicker attention to and treatment of any variation, thereby decreasing the blood loss. We have experienced this ourselves since we commenced the present review.

In previous articles[20, 21] we stated that the blood loss as a result of giving sedation to secure amnesia and analgesia was not materially increased. We admit that our analysis of blood loss was based on a smaller series of cases than the present, and moreover was not as definitely linked up with the various other factors which might influence the volume. In the light of this analysis, our opinion should perhaps be modified in some degree.

We have tried several combinations of drugs, as in Table VIII with varying results. Three hundred and seventy-two patients, or 19 per cent, received no sedative or else nembutal alone, with an average blood loss of 249 c.c. Practically all of these cases were labors of short duration in which the need for sedation was not great. The largest group, 57 per cent, were given nembutal by mouth and paraldehyde either by mouth or per rectum; here the blood loss was increased to 335 c.c. This increase is most marked in the primipara (450 c.c.) but may be due to the large number of episiotomies. A smaller series (7 per cent) received nembutal by mouth and a mixture of paraldehyde and ether per rectum. The resulting average blood loss was increased in primiparas, but decreased in multiparas with a total average of 295 c.c. In the last group in Table VIII where various combinations of drugs were tried (these included nembutal, morphine, heroin, hyoscine, atropine, paraldehyde, and ether) the blood loss was highest. All these cases had long labors due to relative disproportion, soft tissue dystocia, or ineffective labor pains, and consequently resulted in an increased incidence of operative delivery. All these factors were contributory to the increase.

We still believe that sedation has a definite place in the conduct of labor, but our experience has led us to modify our procedure over the course of the years. We have decreased the dosage considerably and changed the time of administration. We believe that comfort or

TABLE VIII. SEDATIVES AND BLOOD LOSS

SEDATIVE	PRIMIPARA		MULTIPARA		TOTAL		P.P. HEMORRHAGE	
	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS	NO.	AV. BL. LOSS
No sedative	10	251	53	266	63	264	8	780
Nembutal alone	67	306	242	229	309	246	30	806
Nembutal and paraldehyde	460	406	683	288	1,143	335	191	854
Nembutal, paraldehyde and ether	66	432	74	175	140	295	27	786
Other combinations	197	365	148	309	345	341	58	773
	800		1,200		2,000		314	

mild somnolence is preferable to unconsciousness, and moreover the peak should be reached during late first stage. During the expulsive stage, the patient can be aided by intermittent gas anesthesia together with local perineal infiltration, thereby decreasing the tendency to atony of the uterus during the third stage.

TABLE IX. BLOOD LOSS IN 100 C.C. GROUPS

AMOUNT IN C.C.	PRIMIPARA	MULTIPARA	TOTAL	%
0-100	107	400	507	25.3
101-200	158	263	421	21.1
201-300	155	169	324	16.2
301-400	80	113	193	9.6
401-500	92	86	178	8.9
501-600	38	25	63	3.2
601-700	67	59	126	6.3
701-800	29	25	54	2.7
801-900	28	23	51	2.5
901-1,000	16	16	32	1.6
1,001-1,500	27	17	44	2.2
1,501-2,100	3	4	7	0.4
Average — 323	800	1,200	2,000	100.0

Table IX and Fig. 1 show an analysis of blood loss in 100 c.c. groups. Sixty-two and five-tenths per cent of all cases show a loss of 300 c.c. or less. The incidence then drops sharply and continues in a gradual slope except for a slight rise in the 600 to 700 c.c. group.

Of the 800 primiparas, 170, or 21 per cent, had blood loss of 600 c.c. or more, as did 144, or 12 per cent, of the 1,200 multiparas. Thus 16 per cent of the total 2,000 patients had post-partum hemorrhage, a much higher incidence than is reported in the literature. On the other hand, if we take into consideration the percentage blood loss rather than the actual volume loss, we find the incidence in primiparas is 14.4 per cent, in multiparas 7.4 per cent, with a total incidence of 10 per cent, a figure much lower and relatively comparable. We agree with Pastore[16] that this is a more reasonable basis on which to grade blood loss and moreover, if agreed upon, will provide a basis of comparison for further investigations.

Closer analysis reveals that the patients with blood loss in excess of 600 c.c. bear practically the same relation to the various factors given in Tables I to VIII as do the total series. What then causes this great increase in total blood loss? In order to examine the problem we pursued our investigation along two channels: first, we carefully reviewed

each hemorrhage case record to find out the several causes or, if possible, the single cause and; second, we planned the study of a series of 150 unselected deliveries on which blood was taken shortly before delivery and during the puerperium with a view to determine blood dilution and recovery consequent to third stage blood loss.

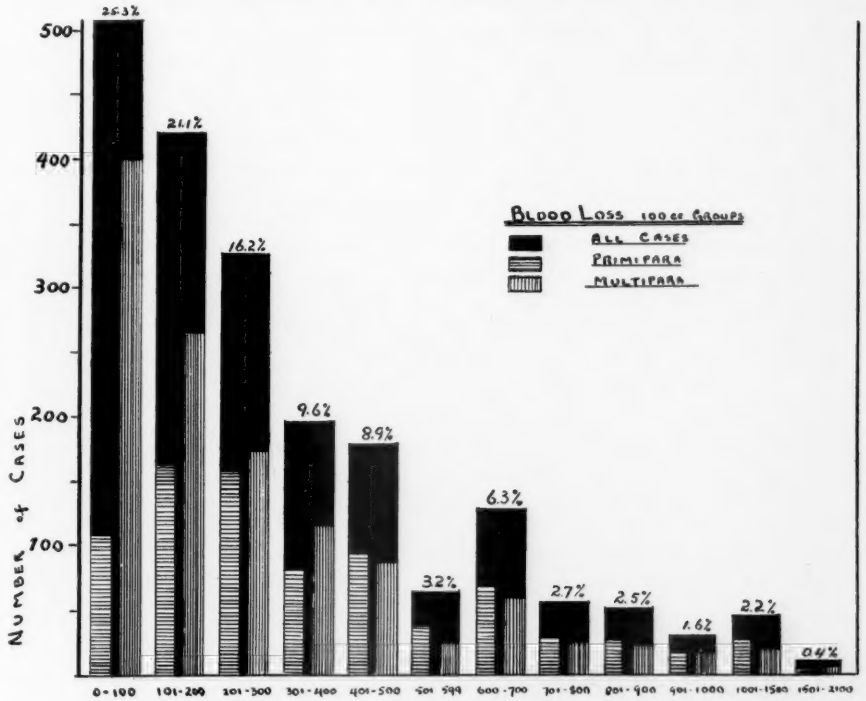

Fig. 1.

In Table X are shown the more common single causes of hemorrhage, of these the largest number (67) are associated with episiotomy, laceration, or repair of a relaxed perineum.

TABLE X. REASONS FOR POST-PARTUM HEMORRHAGE

CAUSE	PRIMIPARA	MULTIPARA	TOTAL
Episiotomy laceration or repair	33	34	67
Instrumental delivery	51	9	60
No reason	26	30	56
Uterine atony	13	28	41
Sedative	16	16	32
			256

Since, of the 314 cases in the hemorrhage group, 126 with perineal wounds lost between 600 and 700 c.c., it is reasonable to suppose that the bleeding from the wound was of itself sufficient to cause their inclusion. This bears out our previous statement and makes us wonder if our very frequent use of incision is always justified. Even with a laceration of the perineum there is but little decrease in the blood loss while the jagged wound is more difficult to repair. We do not advise

enlarging the wound and repairing the relaxed perineum at this time as it definitely contributes to increased bleeding.

In 60 cases, instrumental delivery was judged to be the cause. Twenty-eight were delivered by midforceps application; of these, 21 were arrested occipitoposterior positions, while the remainder were anterior positions which were "tight fits." Associated with forceps delivery in 24 cases was a side wall tear which bled profusely. Low forceps delivery accounted for 32 cases; it would appear that even this operation is not without danger. Perhaps in some instances we might have waited a little longer before resorting to forceps application. A continuing review of our records will no doubt provide the answer.

In 56 cases there seemed to be no obvious reason for the excessive blood loss. In 12 of these, delivery was spontaneous through an intact perineum. The remainder were spontaneous or low forceps delivery, with episiotomy or lacerated perineum. While all the factors previously mentioned were undoubtedly in evidence, it is possible that faulty recording at the time of delivery may have been responsible for our inability to ferret out a single cause for the hemorrhage.

Uterine atony alone or with other lesser causes accounted for 41 cases. Some of these were due to mismanagement of the third stage, others were unaccountable. This might apply to any series.

In 32 cases, sedatives were, we felt, the primary cause. In many instances the total dosage was relatively too great, in others sedative was given too near the time of actual delivery. In the latter instance especially, the result was arrest on the perineum, with a greater incidence of forceps delivery, longer general anesthesia, and atony following delivery. The desirability of having the sedative wear off as delivery approaches, so that the patient may "bear down" to effect spontaneous birth, is evident.

TABLE XI. REASONS FOR POST-PARTUM HEMORRHAGE

CAUSE	PRIMIPARA	MULTIPARA	TOTAL
Twins, large babies, breech	11	9	20
Long labor	15	4	19
Precipitate labor	1	9	10
Premature separation of placenta	1	4	5
Retained placenta	3	1	4
			58

In Table XI the less common causes are noted. In 20 cases the delivery of twins or a large baby was cited as the cause. Associated was a large placenta and the need for greater uterine retraction was quite evident.

Long labor was the cause in 19 cases. Here the usual results of maternal fatigue with operative delivery and atony of the uterus are in evidence. On the other hand, 10 patients were delivered precipitately with resulting hemorrhage. The need for immediate uterine stimulation (probably intravenous ergotrate) is indicated in this complication.

Premature separation occurred as a cause on 5 occasions. An increased loss cannot be obviated in some instances where this complication arises.

In 4 cases the hemorrhage was due to retained placenta; efforts to express it failed. Accordingly, in each case, manual removal was employed.

In this total series there were 30 cases where the third stage lasted longer than thirty minutes but only in 7 was the placenta removed manually. We advise manual removal only when there is profuse or persistent uterine bleeding, where the uterus does not respond to stimulation and where efforts to express the placenta fail. In one case indeed where a thick contraction ring foiled attempts at manual removal, the placenta was left in place. Pelvic examination at six weeks post partum showed a well-involuted uterus; the placenta had apparently become completely absorbed. At no time had there been much bleeding.

Even with the increased blood loss, recovery was in the main uneventful. There were no maternal deaths from post-partum hemorrhage, either at delivery or during puerperium. The general morbidity rate (100.4° F. or over) was 9.6 per cent, while in the hemorrhage group the uncorrected rate was 12.7 per cent. Eighty per cent of these latter patients left the hospital by the twelfth day post partum, while only 7 per cent remained longer than fourteen days.

At the postnatal examination, blood counts in 150 cases were compared with those taken at the first prenatal examination. In 90 per cent the counts were equal to or better than those made at the initial visit. The red cell count averaged 3,900,000 and the hemoglobin estimation averaged 12.5 Gm. per cent.

These are the results of our first avenue of investigation.

Our second avenue, dealing with blood dilution and recovery consequent to blood loss, requires a brief introduction:

Pastore[22] studied the packed red cell volume before delivery and during the puerperium and showed that the cell volume on the third post-partum day varied with the blood loss expressed in terms of percentage of body weight. Using this latter value, he presented data from which the packed cell volume on the third day could be calculated. On this calculation he then based the events which might be expected during the puerperium.

It is now definitely agreed that following an acute hemorrhage, compensation for the decreased blood volume is effected by blood dilution. Plass and Bogert,[23] Stander and his associates,[24] and many others have shown that there is blood dilution during pregnancy. Further dilution consequent to blood loss must then occur immediately following delivery. That compensation for dilution occurs after delivery in many cases is indicated from Pastore's studies, but studies on blood dilution due to blood loss during the third stage of labor seem to be lacking. While such effects might be indicated by red cell volume studies, we felt that these would not give absolute results, since diluted plasma, due to its hypotonicity might affect the size of the cells and as a result the cell volume.

It is now well established that hemorrhage is followed by a decline in the specific gravity of the blood. Since this is due mainly to plasma dilution, it seemed pertinent to examine the specific gravity of the blood serum at certain periods before labor and during the puerperium. Recent developments in methods of estimating specific gravity make

this procedure relatively simple and accurate. Serum was used to avoid errors introduced by an anticoagulant and by hemolysis. In order to balance the study, estimations of hemoglobin, red blood cells, and packed red cells were carried out on whole blood collected at the same time. Blood loss was measured as described and calculated on the basis of percentage of body weight before delivery. Proteins in serum were calculated from the specific gravity according to formula of Weech and others,[25] many results being checked by nitrogen determinations. The results obtained were tabulated according to blood loss in percentage of admission weight and are given in Table XII.

TABLE XII. RELATION OF BLOOD LOSS TO HEMOGLOBIN AND RED CELLS

BLOOD LOSS PER CENT OF WEIGHT ON ADMISSION	HEMOGLOBIN SAHLI GM./100 C.C.			RED BLOOD CELLS MILLIONS/C.MM.			PACKED RED CELLS PER 100 C.C. WHOLE BLOOD		
	1	2	3	1	2	3	1	2	3
0.1	11.7	11.7	13.5	3.83	3.71	4.22	39.6	41.2	46.5
0.24	11.7	11.6	13.3	3.89	3.71	4.21	41.8	40.6	46.1
0.38	11.7	11.7	12.8	3.67	3.67	4.08	40.0	39.8	45.0
0.55	12.1	11.9	12.3	3.79	3.82	4.20	40.0	38.6	46.2
0.63	12.3	11.8	12.2	3.96	3.72	4.03	41.0	38.7	42.6
0.80	11.2	10.5	11.1	3.73	3.45	3.74	39.8	37.3	40.7
0.97	10.1	10.2	11.5	3.63	3.41	3.80	38.6	35.0	41.4
1.06	11.6	9.2	9.9	3.91	3.21	3.62	36.0	30.6	35.5
1.10	10.4	9.0	10.1	3.45	3.26	3.44	39.6	32.6	38.6
1.53	11.6	9.9	10.7	3.83	3.33	3.54	41.3	32.8	38.3

This study is limited to conditions just prior to delivery, twenty-four hours after delivery and on the tenth post-partum day, indicated in the table as 1, 2, and 3. Studies during pregnancy are in progress and will be dealt with in a separate communication.

It will be seen that values for hemoglobin, red blood cells, and packed red cells in the ante-partum specimen bear no definite relationship to the blood loss, apart from being consistently low. Values on the first post-partum day are consistently lower than those of the initial specimen, the difference being most marked where the blood loss exceeds 1 per cent of the body weight. This is best illustrated in the case of the packed cell volume calculated for the third post-partum day, and our findings agree substantially with those of Pastore. Values on the tenth post-partum day indicate the degree of recovery in each group. It will be seen that where the blood loss did not exceed 0.5 per cent of the body weight (approximately 400 c.c.), recovery was complete. If it was in excess of that amount, then the degree of recovery roughly paralleled the blood loss, lesser recovery being related to greater blood loss. That this is not absolute is indicated by the crossed lines in Fig. 2, where, for example, recovery from blood loss of 0.55 per cent of body weight is greater than that from 0.24 per cent, and that from 0.97 per cent is greater than that from 0.63 per cent. The values of the first post-partum day seem much more significant and consistent for that correlation. However, since the absolute differences are so small, it does not seem reasonable to put too great emphasis on these values, except in those cases where the blood loss exceeds 1 per cent of the body weight.

Since the proteins were calculated from the specific gravity, it will suffice to discuss only the specific gravity. Table XIII summarizes our findings for these and correlates them with changes in the packed cell volume. It will be seen that the values in the specimens obtained

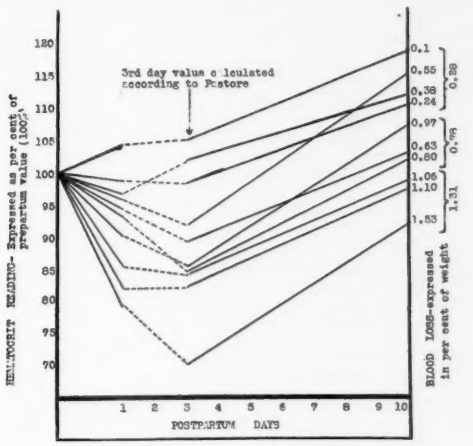

Fig. 2.

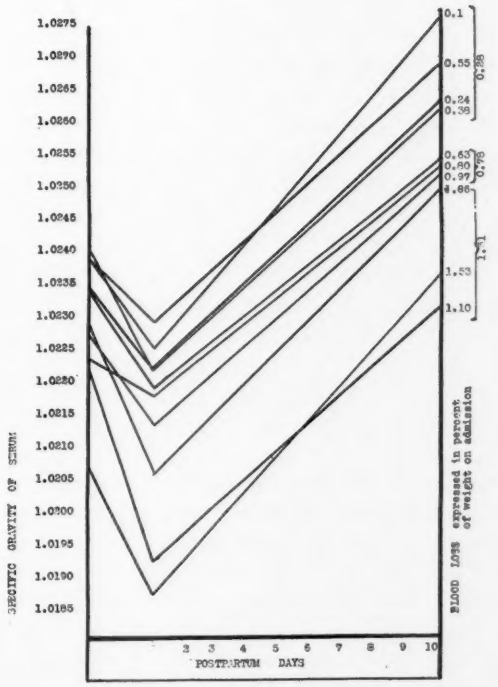

Fig. 3.

before delivery closely parallel the blood loss, and that all are well below the normal value (1.0260-1.0275). The lower the specific gravity, the greater was the subsequent blood loss. So too, the twenty-four-hour post-partum specimen closely paralleled the blood loss and re-

TABLE XIII. RELATION OF BLOOD LOSS TO BLOOD DILUTION

BLOOD LOSS PER CENT OF WEIGHT ON ADMISSION	PACKED RED CELLS IN PER CENT OF ADMISSION SPECIMEN/100%			SERUM SPECIFIC GRAVITY			SERUM PROTEINS GM./100 C.C.		
	2	*	3	1	2	3	1	2	3
0.1	104	105	117	1.0238	1.0225	1.0276	5.75	5.31	7.04
0.24	97	102	110	234	222	263	5.60	5.12	6.58
0.38	99	98	112	239	222	262	5.78	5.12	6.57
0.55	96	92	115	238	229	268	5.74	5.43	6.78
0.63	94	89	103	234	219	254	5.60	5.12	6.33
0.80	93	84	102	223	218	253	5.22	5.07	6.28
0.97	90	85	107	227	213	252	5.38	4.47	6.24
1.06	85	84	98	228	205	249	5.41	4.59	6.13
1.10	82	82	97	222	192	231	5.12	4.14	5.51
1.53	79	70	92	206	187	236	4.62	4.00	5.67

*Calculated for third post-partum day, after Pastore.[22]

flected quite accurately the blood dilution consequent to it. The tenth day values indicated the degree of recovery. This is illustrated in Fig. 3 where values in excess of 1.0260 indicate complete recovery and represent all cases in which the blood loss did not exceed 0.5 per cent of the body weight.

SUMMARY

On the basis of our findings in 150 unselected cases which constituted this part of the study, we feel justified in suggesting that:

1. The specific gravity of the serum obtained within twenty-four hours prior to delivery is a rough index of the extent of blood loss in the third stage of labor. Values exceeding 1.0235 are associated with blood losses not exceeding 0.5 per cent of the body weight. Values in excess of 1.0230 correspond to blood loss not exceeding 1.0 per cent of the body weight. Values below 1.0230 indicate that blood loss in excess of 1.0 per cent of the body weight might be expected.

2. The specific gravity of the serum on the first post-partum day is an accurate index of the blood loss and reflects blood dilution due to blood loss.

3. The tenth day value is an index of the extent of recovery from dilution due to blood loss as well as dilution which occurred during pregnancy.

4. Since both hematocrit measurements and specific gravity estimations indicate that complete recovery from blood loss occurs within ten days of delivery, providing that the blood loss does not exceed 0.5 per cent of the body weight (approximately 400 c.c.) and since complete recovery does not take place in that period by these criteria when the loss exceeds that amount, then a blood loss in excess of 0.5 per cent of body weight should be considered post-partum hemorrhage and adequate treatment instituted.

CONCLUSIONS

We have presented an analysis of 2,000 cases of vaginal delivery with an average blood loss of 323 c.c. In 314 cases (15.7 per cent), there was blood loss of 600 c.c. or more, but only in 205 (10 per cent) was

there a loss exceeding 1 per cent of body weight. Our data confirm the results already established, namely that increased blood loss is related to (1) increase in the weight of the mother, of the baby, and of the placenta; (2) prolongation of labor; (3) operative delivery; (4) laceration or incision of perineum; (5) prolongation of third stage; and (6) ill-judged sedation.

Our data indicate that the commoner causes for post-partum hemorrhage are instrumental delivery, uterine atony, and ill-judged sedation with, as contributory causes, a large baby or twins, long labor, premature separation, or retained placenta. In 56 cases no obvious cause could be attached. The factors concerned in post-partum hemorrhage conform essentially to those already enumerated for the whole group. We have also presented a small series of 150 cases wherein blood dilution as a factor in blood loss was studied. Our data suggest that the specific gravity of the serum obtained shortly before delivery may be used as a rough index of the extent of the blood loss in the third stage and may serve as a warning of an unexpected complication. Since recovery from blood loss judged by serum specific gravity values is complete within ten days, providing the loss does not exceed 0.5 per cent of the body weight (approximately 400 c.c.), it is suggested that any loss in excess of this amount should be considered a post-partum hemorrhage.

With the experience gained in this study, we are confident that we can materially decrease the incidence of post-partum hemorrhage expressed either quantitatively or as a percentage of body weight.

Acknowledgement is made to the Associate Committee on Medical Research of the National Research Council for technical assistance through a grant to Professor G. Hunter.

REFERENCES

(1) *Calkins, L. A., Litzenberg, J. C., and Plass, E. D.:* Am. J. Obst. & Gynec. **21:** 175, 1931. (2) *Calkins, L. A.:* J. A. M. A. **101:** 1128, 1933. (3) *Smith, W. S.:* New York State J. Med. **31:** 141, 1931. (4) *Peckham, C. H., and Kuder:* Am. J. Obst. & Gynec. **26:** 361, 1933. (5) *Brandt, M. L.:* Ibid. **25:** 662, 1933. (6) *Upshaw, C. B.:* J. M. A. Georgia **23:** 55, 1934. (7) *Dieckmann, W. J., and Dailey, E. F.:* Am. J. Obst. & Gynec. **30:** 221, 1935. (8) *Calkins, L. A.:* Ibid. **29:** 231, 1935. (9) *Doerr, E.:* Zentralbl. f. Gynäk. **59:** 22, 1935. (10) *Pastore, J. B.:* Am. J. Obst. & Gynec. **31:** 78, 1936. (11) *Idem:* Am. J. Surg. **35:** 417, 1937. (12) *Abramson, M., and Berman, I.:* Am. J. Obst. & Gynec. **35:** 626, 1938. (13) *Dorset, E. L.:* J. Missouri M. A. **36:** 99, 1939. (14) *Starr, S. H.:* Kentucky M. J. **37:** 120, 1939. (15) *Beecham, C. T.:* Am. J. Obst. & Gynec. **37:** 258, 1939. (16) *Pastore, J. B., and Stander, H. J.:* Texas State J. Med. **35:** 390, 1939. (17) *Smith, R. G.:* J. A. M. A. **111:** 2201, 1938. (18) *Davis, M. E.:* Am. J. Surg. **48:** 154, 1940. (19) *Cosgrove, S. A.:* South M. J. **29:** 1219, 1936. (20) *Conn, L. C., and Vant, J. R.:* Canad. M. A. J. **33:** 484, 1935. (21) *Idem:* Ibid. **35:** 281, 1936. (22) *Pastore, J. B.:* Am. J. Obst. & Gynec. **32:** 859, 1936. (23) *Plass, E. D., and Bogert, L. J.:* Johns Hopkins Hosp. Bull. **35:** 361, 1924. (24) *Stander, H. J., et al.:* Surg., Gynec. & Obst. **31:** 276, 1920; Johns Hopkins Hosp. Bull. **35:** 1, 1924. (25) *Weech, A. A., and Reeves, F. B., and Goettsch, E.:* J. Biol. Chem. **113:** 93, 1933.

DISCUSSION

DR. FRED L. ADAIR, Chicago, Ill.—Hemorrhage is of course extremely important from the standpoint of the deaths it causes, but it also has an effect upon the recovery of the patient which, I think, has not been sufficiently appreciated.

We must, of course, recognize what we might call physiologic blood loss. I do not think anyone would entertain the idea that a woman could be delivered and

not suffer some blood loss, but the question is what is the natural blood loss, and what exceeds it? Dr. Dieckman and Dr. Daily found that on an average the normal blood loss was about 107 c.c., 342 c.c. for forceps operations, and 539 c.c. for cesarean sections.

We have been interested in controlling the blood loss of the third stage and the postpartum period.

We must consider first, however, the physiology or mechanism of the third stage which we believe has not been sufficiently recognized. I have always taught that the third stage consists of two phases. We have the idea that the mechanism of separation of the placenta is due largely to the change in volume of the body of the uterus and that the contraction of the placental segment of the uterus after the baby is expelled is what really effects the separation of the placenta. After the child is expelled naturally the size of the uterus is decreased very materially. It is not until the placental segment of the uterus begins to contract that the placenta separates from the uterine wall thus ending the first phase. By contractions of the uterus it is eventually expelled, completing the second phase of the third stage.

On the assumption that this theory is correct, we have been investigating the use of ergonovine during the third stage. After some trial we finally decided to give intravenous and intramuscular injections of ergonovine as the child was being delivered. We now await the delivery of the head and as the shoulders are being expelled we give an injection of ergonovine, 0.2 mg., as the size of the uterus diminishes with a contraction. This stimulates contractions of the segment under the placental site and facilitates or steps up the first phase, i.e., the separation of the placenta from this segment, so that by the time the child is delivered the separation of the placenta is practically complete and the stage of expulsion follows promptly.

TABLE I. POST-PARTUM HEMORRHAGE, 1,000 DELIVERIES (PRIMIPARAS)

BLOOD LOSS	NATURAL			OPERATIVE		
	2ND	3RD		2ND	3RD	
		IV	IM		IV	IM
500-600 c.c.	0	1	1	1	3	0
600-1,000	0	1	0	0	0	0
1,000-1,500	0	1	0	0	0	0

Table I shows the results in 1,000 consecutive primiparous deliveries both natural and artificial. The amount of blood loss is shown in the left-hand column; the time and the number of cases are shown in the other columns. The natural and operative deliveries are listed separately, and the second and third stages are shown. The method of administration is indicated as intravenous or intramuscular. A corresponding series of multiparous deliveries is shown in Table II.

TABLE II. POST-PARTUM HEMORRHAGE, 1,000 DELIVERIES (MULTIPARAS)

BLOOD LOSS	NATURAL			OPERATIVE		
	2ND	3RD		2ND	3RD	
		IV	IM		IV	IM
500-600 c.c.	0	3	5	0	3	2
600-1,000	0	6	0	0	0	0
1,000-1,500	0	1	0	0	0	0

It is important that the second phase be completed promptly. Otherwise a contracting lower segment may interfere with the expulsion of the placenta. If there is bleeding it is likely to be due to lacerations rather than atony. Occasionally also downward pressure of the uterus causes bleeding by kinking the large veins and producing marked venous stasis. As a rule the longer the second stage and the third stage the greater is the blood loss.

We believe that this method diminishes blood loss, steps up the second stage and promotes shorter and better convalescence of the patient. Furthermore, it has reduced the incidence of manual removal of the placenta and of the other intrauterine manipulations for the purpose of controlling post-partum hemorrhage. For example, in 1936 and 1937 we had 33 uterine packings, and in 1939 and 1940 we had only 2 uterine packings, both because of trauma. The atonic type of hemorrhage has been practically eliminated.

DR. SAMUEL A. COSGROVE, JERSEY CITY, N. J.—Of all of the factors contributing to blood loss in delivery listed by Dr. Conn, I would especially emphasize mismanagement of the third stage. I personally approve the principle involved in the method of keeping the uterus elevated out of the pelvis and expelling the detached placenta from the lower uterine segment by manipulation of that portion of the uterus rather than of the fundus. One cannot, however, be too slavishly addicted to any method. The resourceful obstetrician will modify methods to meet needs. For instance, if there is a tendency for the isthmus of the uterus to contract and incarcerate a separated placenta, only pressure on the fundus will overcome the obstruction and expel the placenta from the uterine cavity.

In our clinic we have run the gamut of injecting pituitrin, the ergot alkaloids, and ergotocin, as each of these several products have become successively available. From time to time we have used both the intramuscular and the intravenous routes. The time of such injections has varied from that of the expulsion of the baby's head through the introitus to the completion of the third stage of labor.

My practice, employed for a period of about a year, is to inject intravenously 1/320 gr. of ergotrate as soon as the baby's head is delivered over the perineum. During the same period of time other chiefs of service in our clinic have followed somewhat different practices. The following are the comparative results obtained by four methods:

	INTRAVENOUS		INTRAMUSCULAR	
ERGOTRATE GR. 1/320	AFTER EXPULSION OF HEAD	AFTER EXPULSION OF PLACENTA	AFTER BIRTH OF BABY	AFTER EXPULSION OF PLACENTA
No. of cases	854	542	81	487
Average duration third stage	7.9	8.7	10.7	8.9
Average blood loss	137 c.c.	170 c.c.	205 c.c.	173 c.c.
Repeated oxytocic necessary	29 cases or 3.3%	14 cases or 2.5%	11 cases or 13.5%	37 cases or 7.5%
Incarceration	17 cases or 1.99%	*5 cases or 0.9%	0	0

*This of course had no relation to the oxytoxic, but when related to the whole group of 1,029 cases (sum of second and third columns), which received no oxytoxic before delivery of placenta, an incidence of 0.4 per cent, it does give a basis on which to assess the incidence when oxytoxic is used as in Column 1.

I further resort more promptly than formerly to manual extraction of the placenta in the event of failure of spontaneous expulsion in response to oxytocics administered as indicated and mechanical manipulation employed. For I have been impressed with the great blood loss represented by apparently insignificant oozing over a period of several hours. Such oozing is never measured nor is attempt very frequently made even to estimate it. The effect, however, on the patient's constitutional condition and subsequent degree of anemia indicates that such blood loss may be astonishingly large and deleterious. I believe that prompt, careful invasion of the uterus is less dangerous than such hemorrhage.

The emphasis placed on certain other factors will vary with the competence of management. Operative delivery per se does perhaps add to the blood loss but hardly to a very large extent if such operative procedures are based on proper indications and conditions and competently carried out. On the other hand, such interference if not judiciously and expertly employed may become a factor in most serious blood loss. Particularly is this so if such ineptness directly causes the lacerations which are such important causes of hemorrhage.

DR. GEORGE KAMPERMAN, DETROIT, MICH.—The measurement of blood loss gives as a rule figures more accurate than mere estimations, but even actual measurement may not be positively accurate. Dr. Conn confesses in his paper that even in making measurements there is a certain amount of estimation. He admits this when he states that the amount of "after waters" usually balances the amount of blood which collects on the linen. We believe these studies have a great academic value, in that they give us certain fundamental information, and it emphasizes facts of which the medical profession is not entirely conscious.

There is a distinct individual variation as to reaction to loss of blood. Patients who lose larger amounts may show little change in their general condition. Patients with smaller blood loss may require transfusion while patients with larger amounts of blood loss may not show such need. Pastore has, however, pointed out that patients with large blood loss may make better post-partum recoveries, if blood is replaced by transfusion, even if at delivery a transfusion may not have seemed urgent.

It has long been our opinion that management of the placental expulsion is the greatest factor in blood loss. The study of Calkins, Litzenberg and Plass did not show that length of first and second stages of labor affected the amount of blood loss, but the report did indicate the importance of the length of the third stage. In Dr. Conn's paper he did not differentiate between the influence of the various stages. Perhaps if he would break down the statistics shown in Table IV it might give a conclusion similar to that of Calkins, Litzenberg, and Plass.

Our earlier teaching was not to interfere with the placenta until a half hour had passed. Now it is recognized, and emphasized by Dr. Conn, that placental separation occurs much sooner. We believe the importance of recognition of placental separation cannot be overemphasized. And we believe it is equally productive of excessive hemorrhage if the removal of the placenta is attempted before separation, as it is if the placenta is not expressed as soon as separation has occurred.

It is not simply a question of waiting, but rather watching and recognizing the signs of placental separation. While the hand on the uterus may be an important factor in preventing hemorrhage by recognizing the condition of the uterine fundus, it all depends on whose hand it is and whether the individual recognizes the purpose of the hand on the uterus. Often this important observation is left to the least trained nurse. Too often the hand indulges in unwarranted massage which may be productive of unnecessary bleeding. In general the uterus should be massaged only when relaxed and bleeding, and not pushed down into the pelvis. Rather it should be displaced upward out of the pelvis.

Some of the procedures of the newer obstetrics may be factors in causing additional bleeding. According to the statistics presented by Dr. Conn, the ordinary outlet forcep, practiced now so frequently with little obstetric indication, is productive of additional bleeding. It all depends on who does it and with what skill and under what conditions the procedure is undertaken. It would seem other factors than low forceps must be the cause of this additional blood loss.

The same comment can be made about the blood loss attributed to episiotomy. We believe the hemorrhage from such an incision should be as controllable as hemorrhage from any surgical incision, and doubtless more so than hemorrhage from a laceration. Furthermore, Dr. Conn reports in 2,000 cases only 5 complete lacerations of the perineum, but each with definitely increased blood loss. Is it not possible that episiotomy in this series of Dr. Conn's may have reduced the number of the more extensive lacerations?

It seems correct to infer from such a study as Dr. Conn has made that the cause of excessive bleeding lies often in certain uncontrollable and unavoidable factors. In such groups the obstetrician's duty is to counteract the results of blood loss and to anticipate this in many instances. We believe blood transfusions should be made more available, easier and should not be so difficult as to be impracticable. The establishment of a blood bank is the best insurance against bad results from hemorrhage. It is significant to note how the number of transfusions increase when a blood bank is available. With a blood bank available, it is just as easy to give a transfusion of blood as it is to give intravenous saline or glucose. We also

would like to emphasize that in the treatment of shock, resulting from hemorrhage, the use of blood plasma in untyped patients is very efficacious and seemingly more so than glucose or saline solution.

A most interesting part of Dr. Conn's paper concerns the study of serum proteins and specific gravity of blood serums. It almost reminds one of the old Calvinistic doctrine of predestination. The amount of blood lost at delivery seems to run parallel to the specific gravity of the blood serum. It seems plausible that one might be able to predict in advance which patients are going to lose blood excessively. We are also impressed by our own experience that patients who are anemic are also more likely to lose blood. The practical inference would be that if prenatal studies of blood could be made, those showing the factors which would prophesy excessive blood loss should be typed in advance and blood transfusions made available.

At Harper Hospital where blood loss is not accurately measured in all cases, and where the label of post-partum hemorrhage is attached because of the clinical condition of the patient, we find 31 such cases among our last 3,000 deliveries. We are well aware that other patients should be included as having had post-partum hemorrhage since doubtless many patients lost 600 c.c. of blood who showed little resulting reaction. Of these 31 patients 21 were primiparas, and 10 multiparas. Eighty per cent were over 25 years of age, 55 per cent over 30 years of age, and 6 per cent over 35 years of age. This means that by far the greater number were below 35 years of age. Among these cases the average primiparous labor was fourteen hours, and that of multiparas seven hours. Sixty-seven per cent had had some type of delivery interference, significantly a percentage far greater than the average percentage of interference in all cases. Of these 31 babies, 58 per cent were 8 pounds or over in weight. In 5 cases the uterine cavity was packed with gauze, and the morbidity among these was the same percentage (20 per cent) as among those not packed. We believe packing the uterine cavity may be resorted to in certain cases without fear of additional morbidity. Eight of these 31 patients had blood transfusions (15 transfusions). Among these cases there were 6 post-partum infections, or 20 per cent morbidity.

While we commend the measuring of blood loss during labor and recognize its importance from an academic standpoint, we do not believe that the delivery of patients without the measuring of blood loss is necessarily poor obstetrics. The recognition of the clinical picture is of greatest importance.

DR. CONN (closing).—Regarding the specific gravity of the serum, we do not know much.

From this small number of cases we do feel that if we get a very low value for serum proteins we would be very careful about giving sedatives. We would not do any episiotomies, would treat that patient very conservatively, and would watch the third stage of labor very carefully. Dr. Douglas, with whom I have been talking, has suggested that by giving plasma to these patients the condition might be changed considerably. This is only a preliminary report, and we are going to study this problem throughout pregnancy to see whether we can arrive at any conclusions.

ECTOPIC PREGNANCY*

Selective Data From Sixty-Five Cases

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ECTOPIC pregnancy appears in our practice and in the general statistics about once in every 200 operative gynecologic cases. It occurs once to about every 300 intrauterine pregnancies.

The material for this study is based upon 65 cases in which the pathologic diagnosis was ectopic pregnancy. Fifty-four of these are from the gynecologic-teaching service of the University of Oregon Medical School, eleven cases from the author's practice. All were seen between January, 1931, and January, 1941. Patients in whom the diagnosis of ectopic pregnancy was incorrectly made are not included.

Age and Parity.—The largest number were noted in the five-year period between 25 and 30 years (17 cases). There were 16 patients between 20 and 25 years; 10 patients between 30 and 35 years; 16 patients between 35 and 40 years. There was one patient under 20 years, one over 40 years.

The incidence in relation to parity reveals that the largest group (26 cases) occurred in patients who had been pregnant once before. The next largest (17 cases) was in patients with no previous pregnancies. In patients twice formerly pregnant there were 13; thrice formerly pregnant, 2; four times, 6. Nothing in these statistics departs notably from common knowledge. The fact that ectopic pregnancy occurred more frequently in women with one previous pregnancy than in previously childless women might argue in a general way against the stated frequency of ectopic pregnancy in women long sterile; nor are statistics relative to age and nulliparity significant. Only one patient in the nulliparous group reported previous treatment for sterility.

Previous Laparotomy, Abortion, Pelvic Infection.—Previous pelvic laparotomies appear to have been frequent in our series; 14 were reported (21 per cent). These figures are rather lower than in most series (Scheffey,[1] Langman and Goldblatt[2]), yet they support the conclusion that previous invasion of the lower abdomen for whatever purpose appears to contribute to the incidence of ectopic pregnancy. In 22 instances (34 per cent), previous abortions were reported, four of which were self-induced. Again this figure supports the evidence that previous abortion contributes to the incidence of ectopic pregnancy. Curettage, for whatever reason, had been done in 10 cases (15 per cent). The question of previous infection, per se, is so bound up in the matter of previous operations and abortions that it could not be separately elucidated. The frequent finding of an inflammatory reaction in the affected tube as well as in the opposite tube removed at the same operation is pertinent. It remains clear that while these factors have been noted somewhat less

*Read, by invitation, at the Sixty-Sixth Annual Meeting of The American Gynecological Society, Colorado Springs, Colo., May 26 to 28, 1941.

frequently in our series than in most (Scheffey,[1] Langman and Goldblatt[2] and others), their frequency definitely points to them as important in etiology.

Symptoms, Pain, Bleeding, Nausea, Fainting.—The patient's first complaint was of pain in 41 cases, bleeding in 19 cases, simultaneous pain and bleeding in five cases. Nausea and vomiting were noted in 38 cases, apparently, however, quite definitely due to the acute illness as distinguished from morning sickness. Interestingly, out of these 38 patients, 13 had fainted, and in each of these 13 cases, rupture and hemorrhage were found to have occurred at or prior to the time of fainting.

Tenderness, Pelvic Mass.—Fourteen patients (21 per cent) complained early of generalized abdominal tenderness; 44 (69 per cent) complained of more or less localized lower quadrant tenderness; 6 (9 per cent) showed definite lower abdominal rigidity; a lower abdominal mass was outlined on abdominal examination in 24 instances (44 per cent); in 10 cases (15 per cent) the finding of a mass was questionable, and in 22 cases (32 per cent) no masses were felt. On bimanual examination a palpable mass was felt in either adnexal region or the cul-de-sac in 38 cases (58 per cent). In 10 instances excessive tenderness prevented satisfactory examination. The estimated size of these masses varied from 5 to about 15 cm. in diameter. Again, these findings do not depart notably from those recorded by others.

Hematology.—Details are available but will not be recorded here. However, certain observations appear justified: Less than 3 million red cells were counted in 14 cases (21 per cent); between 3 and 4 million in 18 cases (27 per cent); and over 4 million in 27 cases (41 per cent). The hemoglobin averaged over 60 per cent in 54 cases (88 per cent). The red count and hemoglobin estimation immediately following or during drastic hemorrhage generally failed to register the true blood depletion. Experience indicates that forty-eight hours must pass before reliable counts are to be expected. A twelve-hour wait appeared to increase the accuracy considerably. Consistently, however, falling red blood count and hemoglobin on repeated analysis reflected serious and progressive intraabdominal bleeding. White counts were increased as they may be expected to be in the presence of hemorrhage. Lilian Farrar called our attention to this phenomenon as long ago as 1925. The sedimentation rate was often accelerated in the presence of hemorrhage and in the absence of infection; and the readings were often as confusing as helpful. We were forced to conclude that the assistance in differential diagnosis usually offered by all of the blood work was too often obscured by the effects of anemia.

Transfusion was done 21 times; 4 times preoperatively, the remainder during or after the operation. Our experience indicates that the decision in regard to the best time to transfuse is absolutely dependent upon the patient's condition. However, except as a definite emergency, it has seemed best to conserve the donor's blood until the bleeding vessels are controlled. Autohemoclysis, wrongly called autotransfusion, was done in five instances, twice on the same patient whose case will be reported (Case 57). Three times it was thought to save a patient's life. We had no unfortunate experience with it. Shaw[3] reports its use 122 times, and Wallingford,[4] 28 times without accident. I believe it is to be recommended in emergencies when more suitable blood is not available. Otherwise, we have had satisfactory results from leaving all blood, including clots.

Concomitant Operations.—In general, we regard as undesirable other operations, particularly elective, performed at the time of operation for ectopic pregnancy. In the presence of hemorrhage or suspected infection, the minimum surgical procedure to control the immediate emergency is called for. Analysis reveals, however, that we have departed considerably from this dictum, and our statistics, therefore, are of unusual interest. Concomitant operations are reported 28 times, including removal of one or both ovaries, both tubes, and all or part of the corpus of the uterus. This material should certainly offer statistics to emphasize the dangers of such practices. However, surprisingly, we find that the average number of hospital days for this group is no higher than for the entire series (nineteen days). The two deaths in our series did not occur in this group and our total death rate (3 per cent) is not out of line.

Recurrent Ectopic Pregnancy.—Incidentally, no patient in our series has returned with a second ectopic pregnancy. This is most unusual and may be due to the fact that so many of the patients were sterilized (18 cases—28 per cent), and had other pelvic pathology attended to. R. B. Smith[5] reported 3.6 per cent second ectopics in 1,608 patients operated upon by members of the American Gynecological Society; others[6-8] report incidences up to 22 per cent. The necessity for later pelvic surgery is frequent as reported in published statistics. These figures then, whatever one's personal convictions may be, must be submitted in defense of conservative surgery indicated on other growths, except in patients with free bleeding or infection. Incidentally, this thesis has its staunch advocates.

The location of the pregnancy in the tube was as follows: 31 (47 per cent) were in the infundibulum; 9 (14 per cent) were in the ampulla; 14 (21 per cent) were in the isthmus. There were one true interstitial pregnancy and one cornual pregnancy. The mass in five instances was apparently extratubal. These were classified as abdominal or broad ligament pregnancies but not so proven. No ovarian pregnancies were noted. The location was not stated in eleven cases. At operation 41 (63 per cent) were demonstrably ruptured and 23 (37 per cent) not ruptured.

Hospitalization.—The average number of hospital days was 16.3 including preoperative and postoperative days. Fifty-two patients were hospitalized less than three weeks (80 per cent); 11 from 21 to 30 days, and 2 patients 31 and 35 days, respectively. These figures coincide roughly with those of Scheffey,[1] Langman and Goldblatt,[2] and others.

Mortality.—There were two deaths in the series, and no deaths in the last eight years. Death occurred in one patient upon whom I* operated, due to peritonitis. An error was made in surgical judgment in the attempt to remove a grossly adherent sac and placenta. The ovular remains should have been left, and the abdomen closed. The second death occurred in a woman who entered the hospital in shock, never rallied and died on the table in spite of immediate transfusion. The mortality rate was 3 per cent.

Diagnosis.—Our diagnosis was correct in 52 instances (80 per cent), and incorrect in thirteen instances (20 per cent). This figure does not include conditions diagnosed as ectopic pregnancy and found not to be. Incorrect diagnoses under which ectopic pregnancy was found at operation included five mistaken diagnoses of ovarian cyst, three of pelvic

*Senior author.

inflammatory involvements and miscellaneous conditions (threatened abortion, ruptured gall bladder, acute pancreatitis, pregnancy in incarcerated retroverted uterus, fibroid uterus with pregnancy). We correctly diagnosed unruptured pregnancy in 13 instances. I believe that our diagnosis has been definitely improved by the routine use of the Friedman test and the frequent use of the cul-de-sac puncture. These will be discussed later.

Ectopic Endometrial Tissue.—Misplaced or aberrant endometrial tissue is occasionally found in connection with ectopic pregnancy. A typical decidual reaction in the capsule of an ectopic pregnancy is frequent, and has generally been ascribed to heteroplasia[9] rather than to the previous presence of true endometrial stroma cells in such an area. It was clearly described in 10 of our cases and doubtless present in more. Frankel and Schenk[10] have been able to demonstrate a decidual reaction in the immediate vicinity of almost every ectopic pregnancy which they have investigated. Langman and Goldblatt[2] in a careful study of their pathologic material were unable to confirm these observations. In one of our cases, Watkins noted and photographed typical decidual reaction in a cul-de-sac endometrioma accompanying an intrauterine pregnancy. In our Case 56, a decidual reaction was noted in an adenomyoma of the Fallopian tube opposite an interstitial pregnancy, and glands were noted in the subserosal myometrium underlying the ovum itself. The evidence here is most convincing of an adenomyomatous area as the cause of arrest of the ovum in this tube (Figs. 1, 2, and 3).

This theory that ectopic endometrium under normal corpus luteum influence may attract and hold the ovum is engaging, and has considerable backing, although the occurrence is doubtless rare. The theory that an abnormally active (nonpregnant) progestational influence may create an unusually receptive nidus for ectopic implantation is also of interest, but also still theoretical. It is indirectly supported by the observations of TeLinde and Henriksen[11] and others, who found almost perfectly developed decidua independent of pregnancy, under hyperprogestational influence, generally accompanying corpus luteum cyst, and often associated with delayed menstruation. May I, at this time, also signalize the basic work in this field done by Litzenberg, at a time when our concepts of the histology of ectopic placentation were very fragmentary.

Corpus Luteum Influence, Increased Progestin Concentration.—The frequent association of corpus luteum cyst with increased progestin concentration may eventually prove to be of interest in relation to the causes of premature implantation. Ectopic endometrium or even simple decidual stroma might theoretically be so affected by this extra progestin as to create an excellent site for premature implantation. However, in our series, among twelve patients with ovarian cyst only four were true corpus luteum cysts, and four single or multiple cystic corpora lutea. Frankel[10] and Ehrhardt[12] both found ovarian cyst in one out of every three ectopic pregnancies, but do not specify corpus luteum cyst. It may also be of interest that in all of the patients with corpus luteum cyst or cystic corpus luteum in our series, the pregnancy occurred in the distal third of the tube, indicating even earlier implantation than usual. These findings are certainly not more than vaguely suggestive, but similar observations should routinely be made in larger series. It must not be forgotten that certain authors (notably Frankel), hold out staunchly for the almost constant etiologic association of ectopic pregnancy with

ectopic decidua. Furthermore, in this connection, the possible danger of the use of massive doses of progestin in the treatment of sterility is to be considered as perhaps predisposing to premature implantation.

Decidual Reaction in the Uterus.—The true endometrium influenced by ectopic placentation theoretically obeys the usual hormonal influences in a perfectly typical manner. It is now well established that the changes which occur after or during the demise of the ovum are in all respects similar, not only to those of menstruation, but, on a relative scale, to those of abortion or miscarriage, and of the third state and puerperium. This matter was discussed before the American Gynecological Society in 1939 after the presentation of a paper by Dr. Harold O. Jones. At this time Drs. TeLinde, Corner, and Schwartz drew attention to the similarity in the behavior of estrin and progestin concentrations.

From the above, certain practical, or we might say, clinical corollaries evolve: (1) So long as the progress of the ectopic gestation is undisturbed, the development of the uterine decidua will follow its usual pattern (minus fetal elements). In two of our cases, one carried to four and one-half and one to five and one-half months, *no* uterine bleeding occurred, precisely as in a normal pregnancy. The more meticulous observers (Veelman, Solomons) have indicated discernible differences in this special decidua, involving chiefly the nature of the gland structure and stratum compactum. There seems however to be general agreement that such differences are minor except for the fetal components. (2) Abrupt death of the ovum, or its operative removal, generally results in early and complete evacuation of the intrauterine decidua, frequently as a decidual cast. Damage to the ovum with gradual disruption of chorionic integrity results in concomitant damage to the intrauterine decidua, generally exhibited as irregular bleeding with partial or delayed disposal of decidua. Jones and Brewer have demonstrated that this process is contingent upon physiologic vascular constriction of the circular arterioles, in all respects similar to the bleeding and disposal mechanism of menstruation.

For use in diagnosis these observations may be conveniently arranged as follows: (1) The passage of an endometrial decidual cast without demonstrable chorionic villi is not only virtually diagnostic of ectopic pregnancy, but generally reflects sudden death of the ovum, spontaneous or operative. Interestingly, a decidual cast was found or reported in seven of our series. Two were discharged a few days after operation, 3 after acute rupture, yet 2 were reported by the patient with the pregnancy unruptured at subsequent operation. (2) Only presumptive evidence of ectopic pregnancy is offered by the finding of decidua in the lochia of suspect irregular bleeding, or by its absence. This is true also of curettings. Naturally, such an investigation is generally in the interest of a differentiation between abortion in progress and ectopic pregnancy. The failure to find chorionic villi in such lochia or curettings cannot be regarded as excluding their presence since the tissue may not have been obtained from the basalis; in other words, placental tissue may be present in the uterus but not in the material for examination; or it may not be found by the microscopist; furthermore, a decision as to the absolute histologic characteristics of the recovered tissue may be impossible.

The decidual reaction in the uterus itself during ectopic pregnancy is chiefly of interest in relation to claims which have been made for the

diagnostic value of curettage. We have had for examination curettings from 6 patients with ectopic pregnancy, the vault of the uterus removed from 8 patients, and 3 decidual casts.* This material has been carefully reviewed with an eye to its potential value in diagnosis. Of these 17 endometriums, only 6 showed a typical decidual reaction; 4 showed hyperplastic endometrium in some areas suggestive of progestational influence; 5 showed normal interval endometrium; one curettage resulted in a dry scrape. These findings cannot be considered even potentially helpful from a diagnostic point of view. In other words, had curettage been done in all of these cases, the diagnosis would have been assisted in only 6 out of 17, and definitely confused in the remainder. Naturally, the finding of chorionic villi in the uterus is diagnostic of intrauterine pregnancy. Yet the finding of decidua in the uterus without villi does not exclude the presence of placental tissue which may have been missed by the curette or by the microscopist. Since, therefore, curettage as a diagnostic measure has some objectionable features under such circumstances, its use should doubtless be restricted.

Aschheim-Zondek or Friedman Tests.—The unsupported statement is too often made that these tests have little or no diagnostic value in ectopic pregnancy. More recent careful observations indicate that, as in intrauterine pregnancy, it reflects accurately the presence of live trophoblast. I am convinced that its more frequent use accounts for the improvement in diagnosis noted in our series in the last four years. Henry Shaw[3] reports the use of the test in 61 cases and finds it reliable. It was made 19 times in our series. Of these 19 tests, 16 were positive. The three negative reactions occurred in patients who proved to have ruptured, nonviable ectopic pregnancy. The test has returned correctly positive in so many cases where there have been bleeding, cramps, signs of infection and other confusing factors, that we are encouraged to rely more upon it as time goes on. Naturally it is useless in differentiating intrauterine pregnancy, and may be confusing in the presence of ovarian cyst.

Briefly, it appears that the Friedman test has helped us as follows: Obviously a positive reaction is significant; but it does not differentiate a disturbed intrauterine pregnancy. A negative reaction does not exclude ectopic pregnancy nor all of its potential danger. I believe, however, that a negative reaction in a case which is not emergent is very helpful indeed. It is understood that the patient's condition, regardless of the negative Friedman reaction, will actually determine the management. A negative reaction, however, in the presence of a questionable diagnosis, may occasionally justify temporizing, and has more than once saved us from entering the abdomen under a mistaken diagnosis.

Colpopuncture.—Puncture of the cul-de-sac for diagnosis has been of signal assistance in our series. Done twelve times without apparent harmful effect, it has yielded conclusive positive results eleven times. A colpotomy was similarly helpful in one instance. In view of general experience, a cul-de-sac puncture by needle seems the more desirable procedure. Preparations for laparotomy should, of course, be complete.

The peritoneoscope was used for diagnosis by Shaw[3] in 11 cases without accident. In 10 cases the blood noted in the pelvis issued from a ruptured ectopic pregnancy. In the eleventh case, hemorrhage from a ruptured follicle was mistaken for that from an ectopic pregnancy. John Ruddock[13] who devised the instrument writes me that he has

*One case was not suitable for microscopic study.

record of 88 examinations with this diagnosis in question. He says the decision was routinely correct and no harm resulted. Recently, with the assistance of Dr. Paul Spangler, I inspected the pelvis of a young woman thought to have a right tubal pregnancy. I saw clearly a large, congested, prolapsed and adherent right ovary with a corpus luteum of pregnancy. The abdomen was not opened and the patient delivered normally seven months later. The procedure is considerably more ambitious than cul-de-sac puncture. It is painful and disturbing to the patient, requires special knowledge and has some dangers. It is difficult to say how important a place it may assume in our diagnostic equipment.

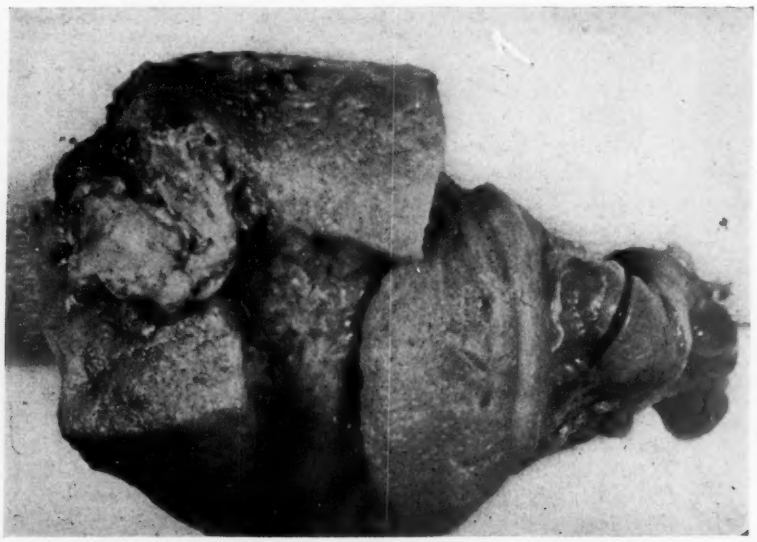

Fig. 1.—(Case 56.) Interstitial pregnancy in right cornu. The tubal structure is completely obliterated and decidual reaction is widespread. Gland structure is demonstrable throughout. The opposite (left) tube contains two lumpy enlargements both hemorrhagic on gross section; both unmistakable adenomyomas of the Fallopian tubes.

CASE REPORTS

CASE 56.—A white female, aged 41 years, gave a history of four spontaneous early abortions, one delivery at term, no pregnancies for seven years. The clinical picture at admission was noncommittal between incomplete abortion and ectopic pregnancy. The Friedman test was positive. Curettage resulted in a dry scrape. The abdomen was opened. The body of the uterus, right tube and ovary and left tube were removed. The right horn of the uterus was the site of a walnut-sized protrusion, incision of which revealed an intact interstitial pregnancy (Fig. 1) surrounded on all sides by gland-containing myometrium. The tubal structure was completely obliterated and decidual reaction was widespread. The opposite tube contained two lumpy enlargements, both hemorrhagic on gross section. These proved to be unmistakable adenomyomas of the Fallopian tube.

Fig. 1 is a photograph of the specimen. The interstitial pregnancy is visible at the right cornu. Fig. 2 is a low power magnification of a section cut obliquely through the right cornu. *Se* indicates uterine serosa; *En* indicates endometrium; *IP* indicates the interstitial pregnancy. The square in the upper left corner is enlarged in Fig. 3, showing unmistakable glandular structure in the subserosal myometrium. Decidua was present in the immediate vicinity. Fig. 4 enlarges the same area.

Fig. 5 is a section cut through an adenomyoma in the opposite (left tube) an inch from the uterine wall. Fig. 6 enlarges the glandular area enclosed by the square, as does also Fig. 7, showing typical adenomyomatous structure with decidual reaction and some inflammatory change.

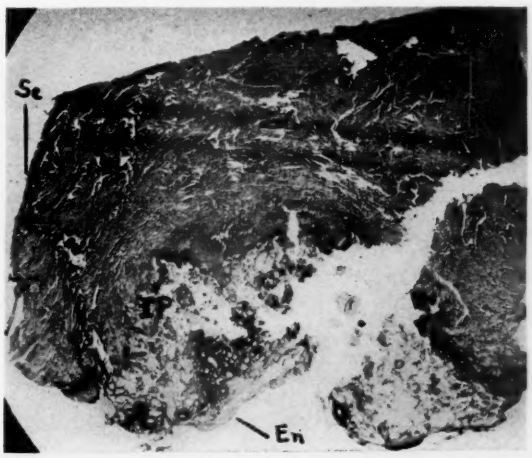

Fig. 2.—(Case 56.) Low power of microphotograph of section cut obliquely through interstitial pregnancy. *Se* indicates uterine serosa; *En* indicates endometrium; *IP* indicates interstitial pregnancy. An area is selected as indicated by the square underlying the serosa in the upper left corner.

Fig. 3.—(Case 56.) Enlargement of enclosed area from Fig. 2. Subserosal endometrial gland.

CASE 57.—A healthy young woman developed what was taken to be a five and one-half months' pregnancy, without pain or irregular bleeding. She was not under my care until she suddenly developed severe pain in the epigastrium which spread rapidly as she went into shock. At laparotomy 1,200 c.c. of blood was obtained for autohemoclysis, over one and one-half quarts being present.

In the pelvis there was a discrete spheroid mass, 15 cm. in diameter, bleeding from a split in its serosa similar to the splitting of the skin of ripe fruit. This tumor was adherent nowhere except at its pedicle (5.0 by 0.5 cm.) which took origin from the posterior aspect of the broad ligament above the mesovarium and below the Fallopian tube. It was clamped and transected with the adjacent portion (middle

third) of the Fallopian tube. Immediate closure was effected. The patient was transfused and recovered without notable event. The sac wall was composed of smooth muscle and connective tissue. Decidual reaction was demonstrable and the lining epithelium was cuboidal. A section of normal Fallopian tube was identified on the anterior aspect of the tumor, 5 cm. in length.

Fig. 4.—(Case 56.) High power of glandular structure underlying the serosa.

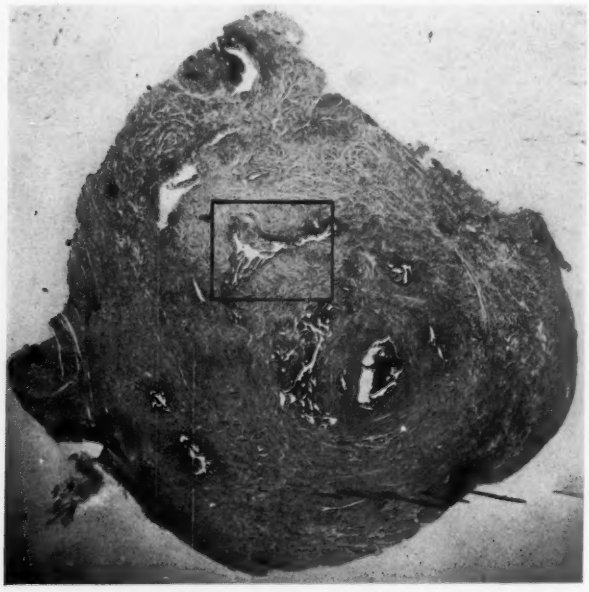

Fig. 5.—(Case 56.) A section cut through an adenomyoma in the opposite (left) tube an inch from the uterine cornu. Tubal lumen is to the right and below the square. The square encloses an adenomyomatous area.

Twenty-four days later, without warning, the patient had another tragic intra-abdominal hemorrhage. Her husband made the diagnosis, reporting by telephone a definite bluish discoloration of the navel which he said made him suspect blood in

the abdomen (the first Cullen's sign, to our knowledge, ever noted by a layman and correctly interpreted). The abdomen was again opened; transfusion and autohemoclysis were performed at once. Blood was found issuing from a large vessel on the dorsum of the right ovary thought to be a recently ruptured follicle. The

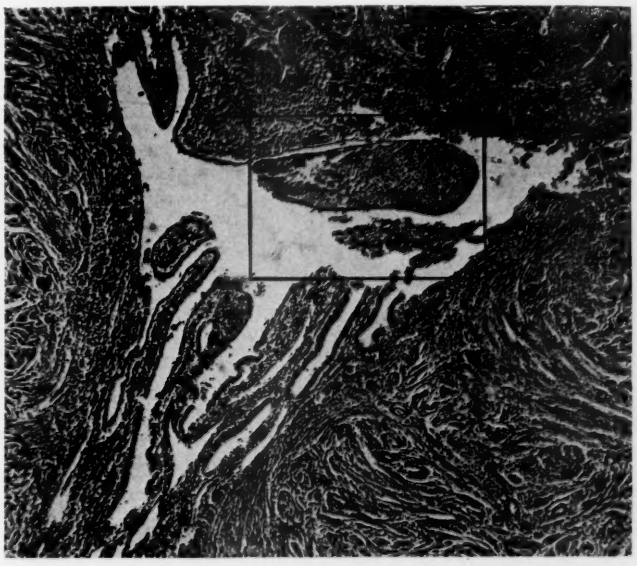

Fig. 6.—(Case 56.) Enlargement of area enclosed by square in Fig. 5. Endometrial glandular structure with decidual reaction and inflammatory change.

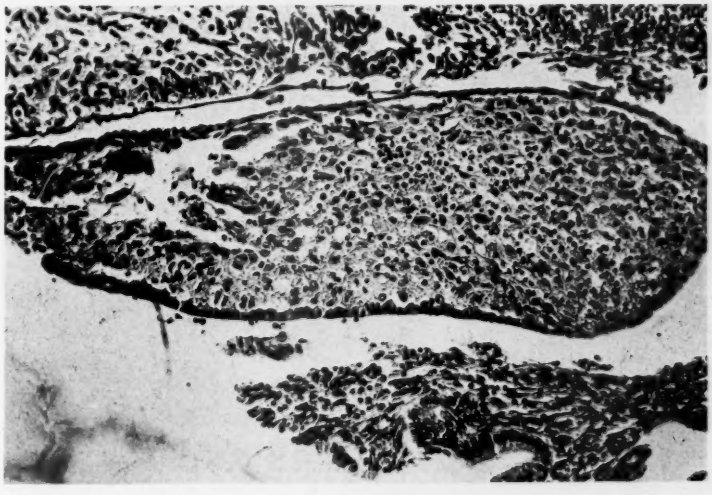

Fig. 7.—(Case 56.) High power showing decidual reaction and glandular structure. This is *not* salpingitis isthmica nodosa.

ovary and remainder of the tube were removed, revealing the proximal and distal ends of the tube intact, and connected by a scarred area in the isthmic portion (portion removed on the tumor at former operation). Recovery occurred without notable event and the patient at the present time (a year later), following a successful tubal insufflation, is normally pregnant at six months.

CASE 58.—A 25-year-old white female, gravida ii, developed an apparently normal pregnancy to four and one-half months. She had no pain, tenderness or other unusual symptoms until four days before operation, when she suddenly developed sharp epigastric pain, later running through the entire lower abdomen. She was operated upon because of signs of intraabdominal hemorrhage. A discrete spheroid

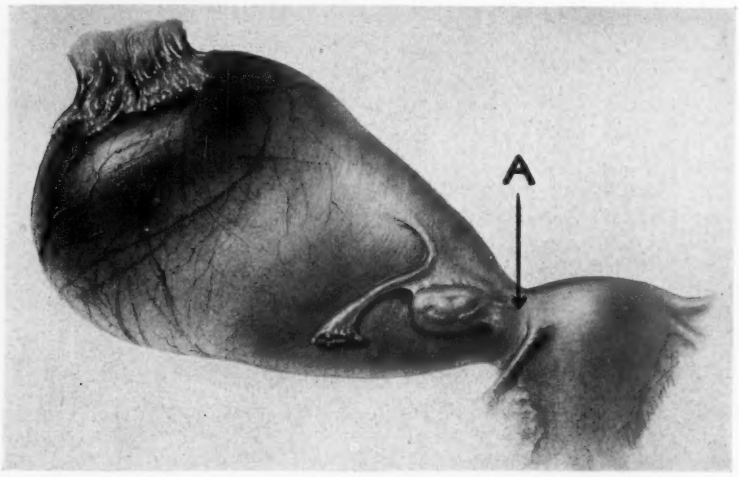

Fig. 8.—A drawing of the ectopic pregnancy from Case 58. The tumor has enlarged posteriorly, bringing the tube and ovary to the front. The distal tube merges with the cavity. No lumen or tubal structure is demonstrable in the pedicle at (*A*).

Fig. 9.—The opened tumor reveals a four and one-half months' pregnancy. The wall was thick, approximately normal myometrium, lined by glandular cuboidal epithelium with definite decidua.

tumor about 8 cm. in diameter was found pedunculated from the right uterine cornu (Fig. 8). The ovary was distal to the mass; the distal end of the tube clearly entered the mass. The pedicle from the uterus measured 1.5 by 4 cm. and on careful serial section revealed typical myometrium with absolutely no evidence of lumen of other connection with the uterine cavity. Fig. 9 shows the tumor opened.

SUMMARY

1. Sixty-five cases with the pathologic diagnosis of ectopic pregnancy are reviewed. For this report some general considerations are omitted in favor of the more pertinent and timely aspect of the problem.

2. The impression that previous operations, abortions, and pelvic infection contribute to the incidence of ectopic pregnancy is supported by our findings.

3. Hematology and blood pressure observations support generally accepted conclusions. Our experience with transfusion parallels that of most other observers. Autohemoclysis, as an emergency measure, has been used with consistent benefit, where more suitable blood is not available.

4. In 28 cases surgery other than removal of the ectopic pregnancy was performed but not in the presence of infection or free bleeding. These patients did exactly as well as the rest of the group. It is thought that this surgical attention may account for the fact that no second ectopics are recorded (28 per cent sterilized). Other reported incidence is 3.6 to 22 per cent.

5. Our mortality rate is 3 per cent. Diagnosis was 80 per cent correct. The routine use of the Friedman test has improved our percentage of correct diagnoses.

6. Seventeen endometriums were available for pathologic examination. Had these tissues been obtained by curettage, diagnosis would have been assisted in only 6 out of the 17 and definitely confused in the remainder.

7. Microscopic examination of the tubes and other tissues indicates some further basis for the hypothesis of ectopic placentation in areas of ectopic endometrium or decidua.

8. Cul-de-sac puncture has been harmless and exceedingly valuable in diagnosis. The peritoneoscope has been used. Its status is discussed.

9. Three unusual cases are reported and illustrated.

Acknowledgement is made to Dr. Raymond E. Watkins for advice and assistance in the preparation of this material; to Dr. Herbert H. Foskett for the histologic studies; and also to Dr. William M. Wilson who operated upon the patient described in Case 58.

REFERENCES

(1) *Scheffey, Lewis C., Morgan, Thomas R., and Stimson, Cheney M.:* Am. J. Obst. & Gynec. **24:** 103, 1932. (2) *Langman, Louis, and Goldblatt, Myron:* Surg., Gynec. & Obst. **69:** 65, 1939. (3) *Shaw, H. N.:* Western J. Surg. **48:** 181, 1940. (4) *Wallingford, Arthur J.:* New York State J. Med. **37:** 1922, 1937. (5) *Smith, Richard B.:* Surg., Gynec. & Obst. **18:** 684, 1914. (6) *Rubin, I. C.:* Ibid. **24:** 443, 1917. (7) *Sserebroff, A. T.:* Arch. f. Gynäk. **364:** 148, Sub., 1932. (8) *Mukuda, T.:* Jap. J. Obst. & Gynec. **20:** 427, 1937. (9) *Marchetti, Andrew A.:* Am. J. Obst. & Gynec. **40:** 69, 1940. (10) *Frankel, J. M., and Schenk, S. B.:* Ibid. **33:** 393, 1937. (11) *TeLinde, R. W., and Henriksen, Erle:* Ibid. **39:** 733, 1940. (12) *Ehrhardt, K., and Kramann, H.:* Zentralbl. f. Gynäk. **60:** 2642, 1936. (13) *Ruddock, John:* Personal communication.

DISCUSSION

DR. DeWITT B. CASLER, Baltimore, Md.—Dr. Schauffler comments on the fact that many of these patients have had previous abdominal operations and many a history of repeated abortions, and he believes that these contribute to the incidence of ectopic pregnancy. I cannot find myself in agreement with this view, but believe that these abdominal operations were probably for previous pelvic inflam-

matory disease, and these abortions had caused a mild pelvic inflammation which in turn was the cause of the ectopic. In my own series of over 300 ectopics, I know of only one case where a previous operation had been the etiologic factor and here a Gilliam suspension had been done and the operator had shortened the round ligament so much that it had caused a definite kink in the tube.

Every one realizes that the extent of the operation performed for an ectopic depends on the location of the pregnancy and the condition of the patient. If the other tube is left in there is of course a definite danger of a second ectopic, as has happened in quite a number of my own cases. Still so many of these women do have normal intrauterine children later, if one tube is left, that it seems unwise to sterilize these patients as a routine measure.

We have had very little help in the diagnosis of ectopics from the Friedman and Aschheim-Zondek tests. At the present time we are having much more satisfactory results with the Falls test. A recent case of unruptured ectopic was diagnosed just twelve days after the patient had missed her menstrual period. The Falls test is much more rapid, taking only an hour for the reaction instead of two days with the others, as well as being much more easily done and less expensive. Most cases of ectopic pregnancy present a sharp, clear-cut picture, with a definite history and clinical findings which make the diagnosis in most cases fairly easy without any laboratory help.

Dr. Schauffler's findings of endometriosis in his ectopics is interesting. This misplaced endometrial tissue may play a much larger part in the etiology of these cases than we now suspect, especially in those cases where there is an adenomyomatous condition of the uterus.

I should like to mention here one fact which to my knowledge does not appear in any of the textbooks and which is of great importance in the diagnosis of ectopic pregnancies which go beyond the early stage. The cervix in abdominal pregnancy corresponds in size and consistency to the pregnancy above it, and not to the size of the uterus itself. This was first pointed out to me by Dr. Kelly and to him should go the credit for the observation. Four members of this Association who were then house officers had examined a patient with a supposed large ovarian cyst and in whom there was no history or suspicion of pregnancy. Dr. Kelly at once pointed out that the cervix was the size and softness of a full-term pregnancy, but the uterus only slightly enlarged. He made an immediate diagnosis from this of a living seven and one-half months' abdominal pregnancy and operated, removing not only the living fetus from its sac, but the entire placenta as well, as it was receiving its entire blood supply from the omentum. Since then this enlargement and softening of the cervix have been found to be present in all of the advanced abdominal pregnancies I have seen. This condition cannot be due in these cases to an increased blood supply as in normal pregnancy, but must be due to some endocrine action of which we as yet do not know.

One further suggestion I should like to make to prevent future trouble is that, even in simple-appearing, unruptured ectopics, tissue should be examined from various portions of the tube so as to pick up a possible chorionepithelioma, as this developed later in one case of my own and was not detected in the single block of tissue cut for diagnosis but found in the block cut later very close to the uterus.

Last, I would like to demonstrate to you an interesting and probably unique specimen (Fig. 1). This patient had missed her period a few days, and while walking on the street was taken with an acute agonizing pain and fell in a collapse. She was taken into a New York hospital, the diagnosis was made of an acute, ruptured tubal pregnancy, and she was operated upon immediately by the Resident. The right tube was removed and a cystic left ovary. Some six years later this patient moved to Baltimore and was referred to me after having experienced a twelve-day delay in her period and then a rather muddy discharge for about fifteen days. She complained of a slight pain in the right side where the previous ectopic pregnancy had been. On examination I could feel a slight enlargement in the cornu of the uterus, and thought that possibly at the previous operation a small stump of the tube had been left where a secondary ectopic had occurred. At operation the following morning I found this unusual condition. The right cornu of the uterus had been resected in New York, and shining through the cornu of the uterus with only a thin

layer of intact peritoneum remaining was an interstitial pregnancy of an early date which was just about to rupture. The ovum of pregnancy had come from the right ovary and then by external migration had crossed over and gone down the left tube into the uterus, and then by internal migration had gone through the uterine cavity up into the right cornu of the uterus to become an interstitial pregnancy. Just why a fertilized ovum should take this circuitous route remains a moot question.

Fig. 1.

DR. LEWIS C. SCHEFFEY, PHILADELPHIA, PA.—My associate, Dr. D. M. Farell and I have reviewed all the ectopic pregnancies that have been observed on the gynecologic ward service at Jefferson Medical College Hospital from Sept. 1, 1921, to Jan. 1, 1941. Our first analysis, published in 1932, included 82 patients; since then 62 additional patients have been observed on the ward service, making a total of 144.

All laparotomies should be taken into consideration when one considers the influence of previous surgery as an etiologic factor in the development of ectopic pregnancy. Appendicectomy in girls and young women, whether or not associated with a suppurative process, is not infrequently followed by peritubal adhesions or occlusion of one or both fimbriae, as demonstrated by insufflation tests in sterility investigations. For the same reason any invasion of the abdominal cavity in the female may initiate conditions favoring ectopic nidation. Thirty-seven of our patients (25.6 per cent) had previous abdominal or pelvic surgery, or both.

I think, however, that abortion, either spontaneous or induced, prior to the ectopic gestation, has a greater incidence. Abortion had occurred in 56 of our patients (38.8 per cent), and in 11 of these it had been induced. Previous intrauterine procedures were recorded in 16 instances (11.1 per cent), and a previous ectopic in eight of our patients (5.5 per cent).

Preliminary curettage was performed in 38 cases (26.3 per cent). This includes patients in whom the diagnosis of ectopic pregnancy was not entertained at the time of operation. In clear-cut cases urgently in need of surgery, the procedure was properly omitted, but in some instances it was performed for investigative

purposes. Decidual reactions were reported in approximately 10 per cent, while the passage of a decidual cast was only established definitely in four instances. We concur with the essayist and others that curettage has a limited and selective value in diagnosis.

Biologic tests for pregnancy have a relative value and are necessarily reserved for differential diagnosis of the suspected case. Previous to 1932, the test was only used twice in our series; both times it was positive and ruptured tubal pregnancies were found. Since then it was employed in approximately 35 per cent of patients with proved ectopics, and in 45 per cent of patients finally evidencing other conditions, but in whom ectopics were suspected.

Of 43 patients correctly diagnosed preoperatively and proved at operation to have ectopics, the test was positive 11 out of 12 times. The negative test occurred in a so-called "old" ectopic. Of 19 patients incorrectly diagnosed primarily, but in whom operation revealed an ectopic, the test was positive 6 out of 10 times. (Two negatives were in suspected pelvic inflammatory cases, one in a supposed retroflexioversion of the uterus and one in a patient regarded as having had an abortion.)

Of 48 patients suspected of having ectopics but later proved otherwise, 21 tests were done of which 14 were negative and 7 were positive. (The 7 positives were all in patients having definite intrauterine pregnancies or complications thereof.) From these observations we think highly of the differential diagnostic value of such tests. The Friedman test has gradually supplanted the Aschheim-Zondek and Mazer-Hoffman procedures.

We are not in agreement with the essayist regarding cul-de-sac puncture, although in his hands it has been of distinct aid in making an accurate diagnosis 11 times out of 12. Successful aspiration assumes that a bulging, fluctuating mass is present in the cul-de-sac, and it seems to us that under these circumstances, colpotomy would be better from the aspect of drainage if pus were to be found, which possibility, in our opinion, is the principal indication for this differential procedure. If a fluctuating mass is not present, we think that aspiration might well damage the intestines. Incidentally we have not performed colpotomy in ten years; prior to that it was done ten times among 82 patients.

We believe that peritoneoscopy offers much in differential diagnosis of especially confusing cases. Dr. Kenneth Fry, of Surgical Service "A" at the Jefferson Hospital in Philadelphia, has developed an excellent technique for the procedure and has rendered us assistance recently in five instances. One confirmed a suspected diagnosis and was followed by immediate operation; four times the procedure revealed, respectively, intrauterine pregnancy, pelvic inflammatory disease, and cystic ovaries (twice). Dr. Fry also diagnosed positively three puzzling cases in which the patient was admitted to the Obstetric Service. We feel that peritoneoscopy is superior to either colpotomy or cul-de-sac puncture, and in our experience it has not been unusually distressing or particularly dangerous in the hands of one familiar with the technique.

Dr. Schauffler is to be congratulated on the correctness of diagnosis in 80 per cent of his patients. We were correct in 75 per cent. Among our incorrect preoperative diagnoses, pelvic inflammatory disease, and incomplete or threatened abortion were the principal conditions thought to be present.

As a matter of additional interest we have analyzed the case histories of 117 patients, admitted to the ward service during the same time, in whom a presumptive diagnosis of ectopic pregnancy was made. Twenty-eight of these patients (23.9 per cent) were operated upon as ectopics. About half of these patients had pelvic inflammatory conditions, the remainder revealing complications of intrauterine pregnancy, ovarian and retention cysts, etc. The sedimentation test has been of little value in differential diagnosis, for rapidity of sedimentation is indicative of tissue destruction; hence it is only "slow" in the unruptured case or where only slight leakage of blood has occurred.

Additional surgery when operating for ectopic is probably unwise, as Dr. Schauffler suggests in mentioning his figure of 50 per cent. Our own figure is 23.6 per cent, and while there were no fatalities in this group, the principle of essential surgery only had better be followed.

In our earlier series, autohemoclysis was performed 15 times, but a death from septicemia influenced us to abandon the procedure, and we have not employed it during the past ten years.

The essayist's mortality, 3 per cent, approximated our own, which is 3.4 per cent for the entire series, but 2.1 per cent in operative cases, since two patients, admitted as emergencies, died before they reached the operating table.

We have encountered but one ovarian and one abdominal pregnancy (probably secondary) in our series.

Gross evidence of endometriosis has been extremely rare in our experience. Histologically it has been reported several times in removed tissues; it is possible that it has been overlooked in some. We did not have time to review all of our pathologic slides but of 62 secured and examined during the past ten years, we found endometriomas in two removed tubes. Of more interest to us was the presence of decidual reactions which we believed were present in 14 specimens. We agree with Novak, however, that the reaction present is usually a "patchy" one, rarely continuous as in the endometrium and often leading to confusion in its interpretation.

DR. ERLE HENRIKSEN, LOS ANGELES, CALIF. (by invitation).—Two statements are often made in regard to the use of the endometrium as an aid in the diagnosis of ectopic pregnancy. These are the following:

1. The decidua-like response without characteristic villi permits the diagnosis of ectopic pregnancy.

2. The absence of a decidual response and the presence of chorionic villi rule out the presence of pregnancy.

The occasional exceptions of which I shall give examples have caused me to lose faith in these rules. Of 11 patients with clinical diagnosis of ectopic pregnancy, 6 were advised to have laparotomy following my report that the uterine curettings revealed decidua without chorionic villi. Four patients were found to have hemorrhagic cysts of the ovary grossly interpreted as being of corpus luteum origin. One patient had an ovarian cyst with a twisted pedicle. One patient refused surgery and was delivered eight months later of a normal child. On the other hand, five of the 11 patients were discharged following my reports that the endometrial responses were not consistent with pregnancy. The patients were later readmitted as surgical emergencies.

We frown upon the use of the peritoneoscope, because it is not the simple instrument or the safe procedure many would have us believe. Its use should be limited to those who not only know the technique of insertion but can also interpret what they see. Cul-de-sac puncture is still our procedure of choice when added information is deemed necessary.

Endometrial, cervical, and vaginal biopsies, vaginal smears, and sedimentation rates have been of little value in our hands.

ON PREDICTING THE LENGTH OF LABOR*

I. First Stage

L. A. Calkins, M.D., Ph.D., Kansas City, Kan.
(From the University of Kansas Hospital)

UNBIASED consideration of the physiologic process known as the first stage of labor would lead one to the conviction that two principal factors should be considered. The motive force is known to be, almost exclusively, uterine contraction. Resistance is provided by the cervix. Very little consideration has been given in obstetric literature to these two major factors in the various discussions of prolonged and difficult labor. Instead, the publications have dealt with age and stature of the mother, size of the pelvis, and size and presentation of the baby. There has been a great tendency to confuse difficult first stage and difficult second stage. We tried to show in our previous publication[1] that there was no correlation between the first stage and second stage and that, therefore, quite different factors must be presumed to govern the second stage from those having to do with the length and relative ease or difficulty of the first stage. We have previously demonstrated with respect to the first stage that such factors as maternal age and stature and pelvic size (within certain limits) do not have a demonstrable bearing on the length of, or difficulty involved in, that process. Infant size has no effect on the duration of the first stage in multiparas and little or no effect on primiparas. Occiput posterior has been said by all observers to result in a somewhat longer first stage than occiput anterior. At the time of our previous publication (1931), it was also our opinion that this was true. More recent information (to be presented in another communication) will prove this view fallacious. Abnormal presentation has been consistently looked upon as one cause of prolonged and difficult labor. Whatever the effect of abnormal presentation on the second stage, there is no particular reason to assume that it would necessarily prolong or otherwise make difficult the first stage of labor. We showed quite conclusively that this was true regarding breech presentation,[1] but the same is not yet settled with reference to bregma, brow, and shoulder presentations. There has been considerable literature with reference to the role of the membranes. Conclusive proof as to the effect of "premature rupture" of the membranes upon the first stage of labor is not yet available.

In a previous publication, we pointed out that variations in consistency of the cervix and variations in frequency and intensity of the labor pains did have an important bearing on the duration of the first stage. It was quite obvious, however, that other factors must also be

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involved. These two variants alone (as analyzed at that time) could not explain either the very short or the very long labors. It gradually became obvious to us that we could not learn what these other factors were without careful examination of a considerable series of patients at the onset of labor and close observation of changing conditions throughout the labor. To see for the first time a patient who has already been in labor several hours does not give us the necessary information as to the conditions present at the time of the onset of the pains and, therefore, leaves us unable to judge what total of work is presented to the uterine forces. In the past few years, we have been making an effort, therefore, to see more patients as their labors begin and to note the relative degree of effacement of the cervix, as well as the dilatation of the external os, the consistency of the cervix, and the station of the presenting point. Balancing this information with the character of the labor pains subsequently observed, we are now able to account for most, if not all, of the variations involved in the first stage. We find ourselves able to predict the duration of the first stage quite accurately. The occasional exceptions can usually be traced to definite pathology.

It should be pointed out that the patient must be seen at the onset of labor. We have found that an examination made the day previous to the onset of labor is not reliable, as in a considerable number of patients quite marked changes take place in the last twenty-four hours before labor begins. We have at present available for study 676 primiparas and 374 multiparas who were seen at the onset of their labors or very shortly thereafter. In a few instances, the primiparas were seen as much as one and one-half (or two) hours after the onset when the uterine contractions had been very weak and infrequent, and it was obvious that no material change had yet taken place. No multipara was included in this group when more than one hour had elapsed since the first discomfort was experienced. These are consecutive cases with no selection or elimination. (A much larger series of patients would have been desirable to prove the thesis to follow, but the conclusions are so clear-cut and the information so readily usable by physicians and students alike that it seemed wise to present the material now.)

DEFINITIONS

Effacement was said to be present (for purposes of this study) when the cervix was either completely effaced or was three or more centimeters dilated (even though there might still be a considerable thickness to the cervical wall). All lesser degrees of effacement were said to be "not effaced."

If the presenting point was at or below the level of the ischial spines, the head was said to be "engaged;" if the presenting point was at any higher level, it was said to be "not engaged."

If the cervix was of the consistency of one's lip, or softer, we called it a "2" cervix; if of the consistency of the ala of the nose, or firmer, we called it a "3" cervix.

In judging the effectiveness of labor pains, we considered intensity and frequency. We did not consider duration as we had previously

shown[2] that duration of the individual labor pain was not important in affecting the duration of the first stage of labor. There is sufficient variation in labor pains, both with respect to frequency and intensity, as labor progresses that one must select a certain time in the labor on which to base his estimate of effectiveness and then try to apply that judgment to the whole of the labor, or the labor must be considered in several segments according to the type of pain present during each of those segments. The latter method is probably too complicated for practical use: The relative infrequency and lack of intensity of the uterine contractions during the effacement phase of the first stage caused us to think that possibly the labor pains should be judged not during effacement but rather at the beginning of the dilatation phase. We, therefore, took as our standard the frequency and intensity of the pains at the time the cervix was either 2 or 3 cm. dilated. We classified the pains as "good," "fair," or "poor," according to the following plan: Good pains were those which occurred at intervals of three minutes or less and with something more than a very weak intensity. Fair pains were those occurring four or five minutes apart with a fair intensity *or* at intervals of three minutes or less but with a very weak intensity. Poor pains were those occurring at intervals of five or more minutes *and* with a very weak intensity.

ANALYSIS OF RECORDS

What might be called completely favorable conditions at the onset of labor would be complete effacement, engagement, soft cervix, and good pains. One hundred thirteen primiparas were in this classification (Table I).

TABLE I. LENGTH OF FIRST STAGE (PRIMIPARAS)

No unfavorable factor
Effaced, engaged, soft cervix, good pains

113 patients—Ave. 3 hr. 17 min.
Range—20 min. to 6 hr. 15 min.

0-6 HR.	6-12 HR.	12-18 HR.	18-24 HR.	OVER 24 HR.
110	3	0	0	0

The average length of the first stage in this group was three hours and seventeen minutes. The shortest was twenty minutes and the longest six hours and fifteen minutes. There were included in this group a small number of patients who had considerable dilatation (four or more centimeters) at the onset of labor. These patients accounted for the very short labors. The majority of patients in this group were in the first stage between two and four hours. It should be noted that no instance of anything like a prolongation of the first stage was noted in this group. A period of about three hours then may be taken as the "basic" duration of the first stage in primiparas.*†

*The scientifically accurate time is perhaps three hours and twenty minutes. This figure is a little more difficult to remember and, as will be developed presently, might be a little more difficult to handle in everyday work. The three-hour period is sufficiently close to be satisfactory for practical purposes.

†Eight patients had a "mushy soft" ("1" on our scale) cervix but their first stage of labor averaged two hours thirty-one minutes, not much less than the average for a "2" cervix.

TABLE II. LENGTH OF FIRST STAGE (MULTIPARAS)

No unfavorable factor
Effaced, engaged, "2" cervix, good pains

53 patients—Ave. 1 hr. 43 min.
Range—5 min. to 5 hr. 35 min.

0-6 HR.	6-12 HR.	12-18 HR.	18-24 HR.	OVER 24 HR.
53	0	0	0	0

Table II shows the similar data for the 53 multiparas in this classification. The usual duration of the first stage in this group is very close to two hours. The average of one hour and forty-three minutes is slightly less, due to the fact that several of these patients also had considerable dilatation at the onset of labor and the average of the whole group was thereby reduced. The "basic" duration of the first stage in multiparas is then about two hours, and the "basic difference" between a primipara and multipara is about one hour.

In the remaining 563 primiparas (83 per cent) and 321 multiparas (86 per cent), one or more of the above four factors (effacement, engagement, consistency of cervix, character of pains) was found to be unfavorable; and the labor, thereby, prolonged beyond the basic three hours for primiparas and basic two hours for multiparas. If two factors were unfavorable, further lengthening of the first stage was observed; three or more unfavorable factors caused a further increase, etc. Carrying this analysis to the limit of the possibilities involved, we were able to develop a table whereby the length of any labor can be predicted with a considerable degree of accuracy.

Lack of effacement adds three hours in primiparas and two hours in multiparas, the same length of time as the basic figures for these two groups (Table IV).

A slightly firmer ("3") cervix also adds three hours (Table V) for primiparas and two hours for multiparas.

TABLE III. PREDICTING THE LENGTH OF FIRST STAGE

		PRIMIPARAS	MULTIPARAS
Effaced, Engaged, "2" Cervix	Good pains	3 hr.	2 hr.
	Fair pains	6 hr.	4 hr.
	Poor pains	12 hr.	8 hr.
Effaced, Engaged, "3" Cervix	Good pains	6 hr.	4 hr.
	Fair pains	9 hr.	6 hr.
	Poor pains	15 hr.	10 hr.
If not effaced add		3 hr.	2 hr.
If not engaged add		1 hr.	1 hr.

TABLE IV. LENGTH OF FIRST STAGE. EFFECT OF NONEFFACEMENT

Primiparas	
Effaced, engaged, "2" cervix, fair pains	6:56
Not effaced, engaged, "2" cervix, fair pains	9:33
Multiparas	
Effaced, engaged, "2" cervix, good pains	1:43
Not effaced, engaged, "2" cervix, good pains	3:19

TABLE V. LENGTH OF FIRST STAGE. EFFECT OF "3" CERVIX

Primiparas	
Not effaced, not engaged, "2" cervix, good pains	6:27
Not effaced, not engaged, "3" cervix, good pains	9:19
Multiparas	
Not effaced, not engaged, "2" cervix, fair pains	6:31
Not effaced, not engaged, "3" cervix, fair pains	8:47

Fair pains (Table VI) likewise require three hours more to dilate the cervix in primiparas and two hours more in multiparas.

Poor pains, on the other hand (Table VII), constitute a more potent factor and, instead of adding three hours to the length of labor when the pains are good, we must add three times three for primiparas and three times two for multiparas.*

TABLE VI. LENGTH OF FIRST STAGE. EFFECT OF "FAIR" PAINS

Primiparas	
Not effaced, engaged, "2" cervix, good pains	6:04
Not effaced, engaged, "2" cervix, fair pains	9:33
Multiparas	
Not effaced, engaged, "2" cervix, good pains	3:19
Not effaced, engaged, "2" cervix, fair pains	5:19

TABLE VII. LENGTH OF FIRST STAGE. EFFECT OF "POOR" PAINS

Primiparas	
Not effaced, engaged, "2" cervix, good pains	6:04
Not effaced, engaged, "2" cervix, poor pains	15:08
Multiparas	
Not effaced, engaged, "2" cervix, good pains	3:19
Not effaced, engaged, "2" cervix, poor pains	9:56

TABLE VIII. LENGTH OF FIRST STAGE. EFFECT OF HIGH STATION

Primiparas	
Effaced, engaged, "2" cervix, good pains	3:32
Effaced, not engaged, "2" cervix, good pains	4:45
Multiparas	
Effaced, engaged, "2" cervix, good pains	1:43
Effaced, not engaged, "2" cervix, good pains	2:34

Lack of engagement is a matter of less importance and apparently affects primiparas and multiparas to the same degree, as we need add only one hour in each group (Table VIII).

Those primiparas having one unfavorable factor are summarized in Table IX. There were 59 patients whose cervices were not effaced but in whom engagement was present, cervix soft, and pains good. The average for this group was predicted to be six hours and was computed at

*Further classes of "very poor" and "very, very poor" pains will be possible in a sufficiently large series. A few such patients in this present series materially increased the averages in the "poor pains" groups in Tables XV, XVII, XIX, and XX.

TABLE IX. LENGTH OF FIRST STAGE (PRIMIPARAS)

One unfavorable factor

			(Predicted)
Not effaced	59 patients	5:59	6 hr.
Not engaged	41 patients	4:23	4 hr.
No soft cervix	17 patients	5:52	6 hr.
Fair pains	30 patients	6:44	6 hr.

0-6 HR.	6-12 HR.	12-18 HR.	18-24 HR.	OVER 24 HR.
94	53	0	0	0

five hours and fifty-nine minutes. There were 30 patients whose cervix was effaced and soft and where the head was engaged but who had only fair pains. The predicted duration of the first stage in this group was six hours and the average found to be six hours and forty-four minutes. Seventeen patients had a firmer cervix but all other conditions were favorable. These "six-hour" patients averaged five hours and fifty-two minutes. Forty-one patients entered labor with the fetal head high but all other conditions favorable, including good pains. The predicted duration for this group was four hours and the average was found to be four hours and twenty-three minutes. It should be noted that there was no instance of a first stage of more than twelve hours in any of these four subgroups. About two-thirds of all these patients had labors of less than six hours and one-third between six and twelve hours.

TABLE X. LENGTH OF FIRST STAGE (MULTIPARAS)

One unfavorable factor

			(Predicted)
Not effaced	16 patients	3:19	4 hr.
Not engaged	49 patients	2:34	3 hr.
"3" cervix	1 patient	2:40	3 hr.
"Fair" pains	11 patients	3:41	4 hr.

0-6 HR.	6-12 HR.	12-18 HR.	18-24 HR.	OVER 24 HR.
75	2	0	0	0

Table X shows the similar figures for multiparas.* Only 2 of 77 patients in these four subgroups had a first stage in excess of six hours. The predicted and computed figures are quite close, considering the small number of patients involved.

TABLE XI. LENGTH OF FIRST STAGE (PRIMIPARAS)

Two unfavorable factors

			(Predicted)
Not effaced, not engaged	67 patients	6:27	7 hr.
Not effaced, "3" cervix	12 patients	8:51	9 hr.
Not effaced, fair pains	28 patients	8:49	9 hr.
Not engaged, "3" cervix	17 patients	6:39	7 hr.
Not engaged, fair pains	26 patients	7:41	7 hr.
"3" cervic, fair pains	7 patients	11:56†	9 hr.

0-6 HR.	6-12 HR.	12-18 HR.	18-24 HR.	OVER 24 HR.
64	79	13	1	0

†Two of these patients had an unusually firm cervix, 16 and 17 hours, respectively.

*In multiparas where the cervix is effaced, relative firmness ("3") of the cervix apparently causes only about one hour increase. Where the cervix is not effaced, the difference is the usual "basic" two hours.

Table XI shows primiparas with two unfavorable factors. The computed and predicted figures are again found to check very closely in each subgroup of patients. In this whole group there were 13 patients with labors of between twelve and eighteen hours and one patient in excess of eighteen hours. Multiplication of unfavorable factors may at times prolong the labor beyond the predicted level. Nevertheless, when it is considered that 143 of these 157 patients had short, or relatively short, labors, the reliability of the index is apparent.

The same data for multiparas (Table XII) show 137 of 139 patients under twelve hours and again a very close reliability of prediction for each subgroup.

TABLE XII. LENGTH OF FIRST STAGE (MULTIPARAS)

Two unfavorable factors

			(Predicted)
Not effaced, not engaged	81 patients	4:16	5 hr.
Not effaced, "3" cervix	5 patients	5:28	6 hr.
Not effaced, fair pains	17 patients	5:27	6 hr.
Not engaged, "3" cervix	9 patients	3:15	4 hr.
Not engaged, fair pains	26 patients	5:20	5 hr.
"3" cervix, fair pains	1 patient	4:00	5 hr.

0-6 HR	6-12 HR.	12-18 HR.	18-24 HR.	OVER 24 HR.
107	30	2	0	0

When three unfavorable factors are present (Table XIII for primiparas and Table XIV for multiparas), the prediction for each individual patient becomes somewhat less exact although for any considerable group of patients the prediction is still very accurate. Sixty-nine patients whose cervices were not effaced and presenting part not engaged and with only fair pains had a predicted duration of ten hours and a computed duration of ten hours and one minute. Two primiparas in this

TABLE XIII. LENGTH OF FIRST STAGE (PRIMIPARAS)

Three unfavorable factors

			(Predicted)
Not effaced, not engaged, "3" cervix	33 patients	9:19	10 hr.
Not effaced, not engaged, fair pains	69 patients	10:01	10 hr.
Not effaced, "3" cervix, fair pains	10 patients	10:52	12 hr.
Not engaged, "3" cervix, fair pains	15 patients	8:30	10 hr.
Poor pains	16 patients	12:29	12 hr.

0-6 HR.	6-12 HR.	12-18 HR.	18-24 HR.	OVER 24 HR.
28	81	24	8	2

TABLE XIV. LENGTH OF FIRST STAGE (MULTIPARAS)

Three unfavorable factors

			(Predicted)
Not effaced, not engaged, "3" cervix	6 patients	6:12	6 hr.
Not effaced, not engaged, fair pains	32 patients	6:31	7 hr.
Not effaced, "3" cervix, fair pains	1 patient	6:10	8 hr.
Not engaged, "3" cervix, fair pains	0		6 hr.
Poor pains	9 patients	7:24	8 hr.

0-6 HR.	6-12 HR.	12-18 HR.	18-24 HR.	OVER 24 HR.
24	21	3	0	0

whole group (represented by Table XIII) had a first stage in excess of twenty-four hours, the first instances of what might be called "prolonged labor." Thus, a labor in excess of twenty-four hours may be considered distinctly abnormal unless at least three unfavorable factors are present in the patient.

Four unfavorable factors bring the primiparas' labor up to thirteen to fifteen hours (Table XV) and multiparas' labor to nine to ten hours (Table XVI). Short labors have now become quite uncommon, and there were five primiparas whose labors exceeded twenty-four hours.

TABLE XV. LENGTH OF FIRST STAGE (PRIMIPARAS)

Four unfavorable factors

			(Predicted)
Not effaced, not engaged "3" cervix, fair pains	26 patients	15:00	13 hr.
Not effaced, poor pains	12 patients	17:25	15 hr.
Not engaged, poor pains	16 patients	11:31	13 hr.
"3" cervix, poor pains	7 patients	13:49	15 hr.

0-6 HR.	6-12 HR.	12-18 HR.	18-24 HR.	OVER 24 HR.
3	19	27	7	5

TABLE XVI. LENGTH OF FIRST STAGE (MULTIPARAS)

Four unfavorable factors

			(Predicted)
Not effaced, not engaged, "3" cervix, fair pains	14 patients	8:47	9 hr.
Not effaced, poor pains	9 patients	9:56	10 hr.
Not engaged, poor pains	12 patients	9:00	9 hr.
"3" cervix, poor pains	0 patients		9 hr.

0-6 HR.	6-12 HR.	12-18 HR.	18-24 HR.	OVER 24 HR.
9	18	7	1	0

Five unfavorable factors (Tables XVII and XVIII) show a disappearance of the short labors (six hours) for both primiparas and multiparas, and an appearance of an appreciable proportion of primiparas in excess of twenty-four hours.

TABLE XVII. LENGTH OF FIRST STAGE (PRIMIPARAS)

Five unfavorable factors

			(Predicted)
Not effaced, not engaged, poor pains	25 patients	23:00	16 hr.
Not effaced, "3" cervix, poor pains	7 patients	24:53	18 hr.
Not engaged, "3" cervix, poor pains	7 patients	17:46	16 hr.

0-6 HR.	6-12 HR.	12-18 HR.	18-24 HR.	OVER 24 HR.
0	6	12	12	9

TABLE XVIII. LENGTH OF FIRST STAGE (MULTIPARAS)

Five unfavorable factors

			(Predicted)
Not effaced, not engaged, poor pains	12 patients	11:48	11 hr.
Not effaced, "3" cervix, poor pains	0 patients		12 hr.
Not engaged, "3" cervix, poor pains	0 patients		10 hr.

0-6 HR.	6-12 HR.	12-18 HR.	18-24 HR.	OVER 24 HR.
0	4	6	2	0

Six unfavorable factors (Tables XIX and XX) show for primiparas a labor in excess of twenty-four hours to be the rule and therefore normal. There were no labors less than twelve hours. The one multipara whose labor was less than six hours probably represents an error in the initial recordings on this patient.

TABLE XIX. LENGTH OF FIRST STAGE (PRIMIPARAS)

Six unfavorable factors

Not effaced, not engaged, "3" cervix, poor pains	16 patients	29:37	(Predicted) 19 hr.

0-6 HR.	6-12 HR.	12-18 HR.	18-24 HR.	OVER 24 HR.
0	0	5	2	9

TABLE XX. LENGTH OF FIRST STAGE (MULTIPARAS)

Six unfavorable factors

Not effaced, not engaged, "3" cervix, poor pains	9 patients	13:57	(Predicted) 13 hr.

0-6 HR.	6-12 HR.	12-18 HR.	18-24 HR.	OVER 24 HR.
1	2	5	1	0

DISCUSSION

It should be noted that the management of this series of patients did not include heavy sedation for any first stage. Nitrous oxide oxygen with small doses of morphine (on indication only) were the only means of sedation employed. Other patients delivered in the hospital during the same period and to whom heavy sedation was given had much longer labors. One patient only was excluded from this series because of a pathologically hard cervix. In one patient only a small pelvis might have had a deterrent effect on the course of the labor. This patient was a multipara for whom a thirteen-hour labor was predicted, and she was not completely dilated until the end of seventeen hours. Her conjugata vera was estimated at 8.5 cm. Whenever a patient developed a secondary inertia with no pains for a period of several hours, that painless period was not counted in the total duration of her labor. The number of induced labors was too small for us to tell whether the induced labors were either shorter or longer than those occurring spontaneously. The same can be said with respect to premature rupture of the membranes.

SUMMARY

Table XXI shows in simple form a method for predicting the duration of the first stage of labor with the percentage likelihood of the occurrence of "good," "fair," and "poor" pains so that, with any given patient, the likely duration can be quite readily determined even in advance of any labor pains. As soon as the first dilating pains appear, the patient can be completely catalogued and the time of complete dilatation readily determined.

This knowledge is of importance in several ways. If a long labor can be predicted, the need of maintenance of free food and fluid intake is

TABLE XXI. PREDICTING THE LENGTH OF FIRST STAGE

		PRIMIPARAS	MULTIPARAS
Effaced Engaged "2" Cervix	Good pains 63%	3 hr.	2 hr.
	Fair pains 25%	6 hr.	4 hr.
	Poor pains 12%	12 hr.	8 hr.
Effaced Engaged "3" Cervix	Good pains 45%	6 hr.	4 hr.
	Fair pains 33+	9 hr.	6 hr.
	Poor pains 22%	15 hr.	10 hr.
If not effaced add		3 hr.	2 hr.
If not engaged add		1 hr.	1 hr.

obvious. If a short, easy labor can be predicted, the need for operative intervention in certain types of pathology is obviated. It is high time that labors should be judged on the anatomic and physiologic factors in the genital tract rather than on "manufactured dicta" as age and stature of the whole body. It is also important, if the labor goes definitely beyond the predicted limits, that careful search for unrecognized abnormalities should be instituted without delay.

Finally, it is interesting to speculate on the etiology of the variations in the cervix and in the uterine contractions. The cause is not anatomic; it is almost certainly physiologic. There is some evidence that variation in the cervix may produce variation in the uterine contractions and vice versa. The etiology of the onset of labor is inextricably involved in both. Further research is obviously necessary. Only when we find this physiologic factor can we hope to so "prepare" the least favorable patients in advance that they may enter labor with unresisting cervices and good uterine contractions.

REFERENCES

(1) *Calkins, L. A., Litzenberg, J. C., and Plass, E. D.:* AM. J. OBST. & GYNEC. **22**: 604, 1931. (2) *Calkins, L. A.:* Ibid. **27**: 349, 1934. (3) *Calkins, L. A., Irvine, J. H., and Horsley, G. W.:* Ibid. **19**: 294, 1930.

1010 MEDICAL ARTS BUILDING

DISCUSSION

DR. FRANCIS C. GOLDSBOROUGH, BUFFALO, N. Y.—One or two points Dr. Calkins has emphasized are quite important. (1) The position of the child plays very little part in the way in which the cervix dilates. (2) It is important to see the patient as soon as the pain begins. We too frequently see her only after she has been in labor for a few hours and there is some effacement and some dilatation. One of the main points Dr. Calkins brought out is that we should know the condition of the cervix when labor starts in order to gauge progress.

I am a little uncertain as to what is Dr. Calkins' definition of the onset of labor. It seems to me the average duration of his first stage is rather shorter than most of us have been led to accept, and I am wondering whether he sets the onset of labor as the time when the cervix is effaced or when the patient first complains of painful contractions of the uterus?

Dr. Calkins has brought out a very interesting method by which we may predict with some satisfaction the duration of the first stage of labor. As we all know that is the stage during which the family are requesting that something be done for the patient. With too much urging very frequently intervention is undertaken which may be harmful both to the mother and child. With this knowledge we might be more able to pacify them.

DR. GEORGE W. KOSMAK, NEW YORK, N. Y.—After having read the paper and heard it presented this morning I feel that there is considerable practical value in it, and one of the very sensible things is keeping up the spirits of the patient during a period that is not always predictable. If Dr. Calkins has the formula that will give us some information, we may be able to do more for our patients. I hope he will keep on with this study and give us a formula for the second stage so that we may pacify not only the patient but the family as well.

I wonder how much the question of sedation is going to enter into this. Dr. Calkins has plainly indicated he feels that in some patients sedation will prolong the duration of labor. I think there would be great difficulty, however, in convincing the public and the patient sufficiently so that it would lead to an elimination of sedative measures. These academic questions constitute one of the important problems to which the obstetrician should pay attention and attempt to solve.

DR. G. D. ROYSTON, ST. LOUIS, MO.—I would like to ask whether these observations were made personally by Dr. Calkins or by one of his subordinates?

DR. OTTO H. SCHWARZ, ST. LOUIS, MO.—The labor was definitely prolonged where sedatives were used. At what stage was the sedation first begun?

DR. NORMAN R. KRETZSCHMAR, ANN ARBOR, MICH.—I would like to ask Dr. Calkins to explain when and how he evaluates the pains. From the subjective reaction of the patient, one never knows when she is having a good pain nor does palpation seem to give definite evidence of the quality of the pains.

DR. NORMAN HARRIS WILLIAMS, BEVERLY HILLS, CALIF. (by invitation).—What is Dr. Calkins' definition of the termination of the first stage of labor?

DR. J. MALDONADO, SANTE FE, N. M. (by invitation).—I would like to ask what effect the presenting part has on the pains?

DR. WILLIAM J. DIECKMANN, CHICAGO, ILL.—Are the dilatation and the consistency of the cervix based on rectal or vaginal examination?

DR. CALKINS (closing).—Dr. Goldsborough asked at what time we estimated the efficiency of the labor pains. The answer is, just as soon as we know the cervix is beginning to dilate. We have to wait until it is 2 or 3 cm. dilated because we wish to estimate the pains during the dilatation phase and not during the effacement phase. Labor begins whenever the patient experiences her first discomfort.

Dr. Royston asked by whom the observations were made. A small proportion were made by myself, the majority by my resident, and a few by my intern. My senior students can make these observations just as accurately and predict the labors just as satisfactorily as we indicated in this paper.

Dr. Schwarz asked at what time those few patients had received their heavy sedation. In most instances at a dilatation of about 4 to 6 cm.

Dr. Kretzschmar asked about the evaluation of pains with relation to their intensity. Of course, the method we used is very crude but it seems to work. If we can depress the uterine wall very markedly during the contraction, that contraction is very weak. If we can depress it moderately, that is a fair contraction; if not at all, it is a very firm contraction. That is the only method we employ and we think that it is all that is necessary. It must be taken, however, in conjunction with the frequency of the pains. One or the other alone is not sufficient.

Dr. Williams asked when we consider the first stage terminated. When we can no longer feel the cervix. If it is within reach of our rectal examining finger, we feel that it still can be holding the presenting part and the first stage is not over. When it has completely retracted we consider the first stage completed.

Dr. Maldonado asked what effect the presenting part may have on the pain. It was stated in a previous paper to have had no effect whatever in the first stage.

In answer to Dr. Dieckmann, 97 per cent of our examinations were rectal. A vaginal examination is done whenever we feel that the information is incomplete or otherwise unsatisfactory.

VARIABLE SIGNIFICANCE OF HEARTBURN*

NORMAN H. WILLIAMS, M.D., BEVERLY HILLS, CALIF.

OF ITSELF the frequency of heartburn during pregnancy gives distinction to the ailment. Never serious as a threat to health, even a mild degree of heartburn, if persistent, will lower personal efficiency in meeting the responsibilities of daily life; while intense heartburn at night will banish sleep completely. Of these consequences prospective mothers complain, and from them ask relief. Household remedies may suffice; but not always. Indeed, intractable cases continue to baffle physicians. And logically enough, members of the medical profession from time to time delve into the problem clinically and experimentally seeking the cause for and the cure of this annoyance common among both men and women; and especially likely to occur during pregnancy.

INCIDENCE

Some degree of heartburn, slight or severe, is associated with two-thirds of the cases of pregnancy, irrespective of the age or parity of the subjects. It makes its appearance at any time during the period of gestation. In a statistical survey, Rodway and Shelley noted the following distribution of the cases they observed: 15.1 per cent during the first four months of pregnancy, 20.2 per cent in the fifth month, 45.5 per cent between the sixth and eighth months, 18.2 per cent in the ninth month. Most intense during the later months the discomfort was often described as torture.

CAUSATION

High-strung individuals are predisposed to heartburn. But those who have a placid temperament experience it notably when under mental strain. It has been called "the student's disease," because so often it is the penalty of consistent mental concentration. There incidentally lies a hint of the nervous factor concerned.

Diet, too, plays a role, well defined, if not leading. Drinking water in suitable amounts, avoiding sweets, pastry, fatty food, and acid beverages are believed to be preventive measures; while milk and the use in general of a high protein diet have been recommended as curative.

Gastric hyperacidity was accepted for a long time as the explanation for the ailment. Accordingly pregnancy, it was assumed, promoted the secretion of hydrochloric acid excessively; an interpretation that had clinical support. Each of us, not unlikely, has witnessed the grateful attitude of patients advised to counteract what was thought to be gastric hyperacidity by neutralization with an alkali, salts of sodium, magnesium, or aluminium. To the rule, however, there were notable

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exceptions, and sceptics of alkali therapy multiplied after Kehrer in 1905 announced that both combined and free hydrochloric acid are actually below normal in the gastric secretion of pregnant women. Ample confirmation of his analyses has come from many laboratories. An admirable study made by Strauss and Castle in this country contributes substantially to the chemistry involved. Now, it has been established that gastric acidity decreases as pregnancy advances, being lowest in the third trimester when heartburn becomes most prevalent and severe. Following the act of birth, along with the disappearance of heartburn, gastric acidity mounts and its height may treble that of the ante-partum level.

Chemical analysis of the gastric juice inevitably shook the foundation of alkaline therapy, encouraged accurate definition of the secretion by quantitative methods and pointed to the use of hydrochloric acid in cases of heartburn. Promptly the reports of Mason and others proclaimed the relief during pregnancy by this treatment. But before long the need for discrimination was emphasized in recommending any form of medication to alter gastric acidity.

For example Rayner in 1933 recognized three groups in a series of 45 pregnant women suffering from intractable heartburn; first, those who were relieved by acids; second, those who were relieved by alkalis; and third, those in whom the symptom was aggravated by acid and was not relieved by alkali. Similarly Rodway and Shelley two years later in the course of forty gastric analyses upon pregnant women found a low or moderate degree of acidity in twenty-four, and a high degree only in three instances.

It is pertinent that these investigators noted the eventual development of a toxemia in 7.5 per cent of the women who earlier had complained of heartburn. That association encouraged some obstetricians to employ a salt-free diet routinely whenever heartburn became a major complaint. The results were not uniform, as would be expected now that we understand the basis of the disturbance not to be chemical but mechanical, an upset in gastrointestinal dynamics.

IMPAIRMENT OF NEUROMUSCULAR MECHANISM

Experimenting with a technique previously employed by Bloomfield and others, Chester Jones localized a number of pathologic manifestations pertaining to the gastrointestinal tract.

He learned that heartburn is derived from spasm of the cardiac sphincter of the esophagus. This was proved by the manipulation of a small distensible balloon attached to a fine rubber tube which was swallowed by subjects of the experiments. The bag's position was followed downward step by step from esophagus to rectum with the help of fluoroscopy. Symptoms caused by pressure of the balloon, inflated at intervals, were accurately localized. The initial observation identified the lower end of the esophagus as the area responsible for heartburn. The pressure of the balloon against the area caused the sensation of burning. "In a few instances the subjects felt as if something sour or hot was being carried upward toward the mouth, simulating the symptom, acid regurgitation."

Subsequent experiments demonstrated that the sensation in question could be reproduced by the introduction of fluids poured into the esophagus through a catheter. And, amazing fact, the composition of the fluid did not matter. What counted was the irritation of the esophageal mucous membrane, a reaction elicited by bland solutions, even warm or cold water. Specifically, the following materials caused heartburn: Cold water in eight experiments, warm water in three, N/10 HCl in five, N/10 NaOH in six, barium sulfate in one, the subject's own gastric juice in two.

Jones's observations warranted conclusions with respect to heartburn which may be summarized briefly. The chemical composition of the fluids concerned is of less importance than their quantity and the rapidity with which they are introduced into the esophagus. Constriction of the cardiac sphincter, exquisitely demonstrable when barium solution is used, prevents passage of the material. This inhibition is followed by waves of reverse peristalsis which carry the fluid upward. Furthermore, coincident with the disappearance of retroperistaltic waves the discomfort ceases. Accordingly for the relief of heartburn, the administration of atropin to relax the neuromuscular mechanism involved represents a logical type of treatment.

GASTRIC CHANGES INCIDENT TO PREGNANCY

We must examine next the physiologic changes resulting from the influence of pregnancy upon the gastrointestinal tract. Current methods of investigation have clarified at least three cardinal facts, namely, changes in the position, in the musculature, and in the motility of the stomach.

Normally the stomach is in a vertical position, the lesser curvature to the right approximately parallel with the spinal column and the cardia opposite the tenth dorsal vertebra. The alterations consequent upon pregnancy plainly depicted in the diagrams of Hansen have been verified by our own radioscopic studies. As would be expected, the encroachment of the pregnant uterus upon territory formerly occupied by other abdominal organs slowly increases until near term when the topographic transformation becomes maximal. Then the fundus of the stomach has been pushed upward into the left diaphragmatic cup. Simultaneously the axis of the stomach has been rotated to the right approximately 45 degrees. Also the greater curvature has approached the cardia. This horizontal position hinders the stomach in emptying itself.

Added to the changes in the position is atony of the stomach musculature which allows the organ to lie flaccidly against the enlarging uterus. This atony affects the cardiac sphincter and often the esophagus as well, which may permit hiatus herniation. Access of gastric juice to the lower esophagus is thereby favored. Clinically this explains why many patients complaining of heartburn discover the symptoms exaggerated when the body posture is recumbent or when effort is made to sit up from the reclining position. Fetal movements, too, may produce this discomfort.

Diminished motility of the stomach is a constant physiologic condition in pregnancy. Normal persons, according to Guthman, have an emptying time of two hours, whereas during pregnancy Hansen found this

period prolonged from fifty to one hundred and thirty minutes. In a few pregnant women the stomach never emptied itself completely. In general, motility decreases directly with the acid content, presumably an explanation for the benefits following the administration of hydrochloric acid, already mentioned. Knowledge to what extent gastric motility depends upon endocrine influence is still wanting. Experimental evidence thus far has been derived only in respect to the thyroid. In their studies Morrison and Feldman have clearly demonstrated a positive relationship between this gland and gastric retention, a relationship independent of the vagus.

With these gestational variations in mind it has seemed reasonable to try to reduce the neuromuscular theory of heartburn, as it may pertain to pregnancy, to factual observations. While investigations are still in progress, they have reached a point where a few conclusions may be expressed with confidence. However, since the work began a number of questions have arisen which cannot be answered at the moment.

OBSERVATIONS

We have studied pregnant women by means of x-ray plates and fluoroscopy, both those with and those without heartburn. With the thought of possible damage through repeated x-ray exposures, our observations have been curtailed and the data with respect to a single individual rendered less extensive than final solution of the problem requires. Nonetheless we have already witnessed results with helpful clinical implications.

Initially a 200 c.c. barium meal was given and its propulsion followed through the esophagus. Its behavior in the stomach was watched for a period believed to be within the limits of safety. And, indeed, proved to be so. In these circumstances there was opportunity to note evidences of such phenomena as hiatus hernia, esophageal dilatation, regurgitation, and reverse peristalsis whenever the patient was a victim of heartburn. If not, the observations contributed information relative to the anatomic relations in pregnant women having no digestive complaints, normal cases so to say.

These normal cases left no doubt that the stomach regularly suffered encroachment by its neighbors during pregnancy, was pushed upward to the left and occupied the diaphragmatic cup on that side. No changes appeared in the lower esophagus or cardia, excepting one instance in which there was well-developed hiatus hernia.

Likewise, in seven cases of heartburn, there were no pathologic alterations radioscopically visible. On the other hand in three cases of heartburn there was moderate dilatation of the lower third of the esophagus, in one case the passage of barium was delayed at the cardia with a slight amount of regurgitation, and only in one instance was a hiatus hernia discovered; this, with dilatation above it. Evans and Bousling describe hernia of this type in two cases of intractable heartburn. Such revelations as these imply that the clinical symptom, heartburn, rarely rests upon an anatomic basis and that for the most part its origin and development lie within the domain of pathologic physiology. This

conclusion, of course, represents no novelty, for Chester Jones and others have convinced most of us, at least, that heartburn is essentially a neuromuscular phenomenon.

Granted this premise and assuming the mechanism to a degree analogous to disturbed intestinal tone in certain postoperative cases, it seemed that the use of prostigmin would have a rational basis as a therapeutic means of relieving the symptom. Accordingly injection of 1 c.c. of 1:2,000 of prostigmin was tried, cautiously, to be sure, until certain it was safe to use the drug in the course of pregnancy. The limited number of our observations does not permit an unqualified conclusion. The results, however, are sufficiently noteworthy to suggest a need for further trial.

Among 16 patients with severe heartburn treated with a single dose of prostigmin one was not benefited, 14 were made comfortable or entirely relieved within twenty-four hours. In about half of these cases the distress gradually recurred in from seven to ten days. A second dose proved as effective as the first. By repetition of the injections these patients were kept free of the symptom with no untoward results.

RECAPITULATION

Dietary and other kinds of hygienic indiscretion may provoke heartburn. Sometimes dosage with alkalis affords relief, implying the presence of gastric hyperacidity. Chemical analysis, however, challenged the correctness of that interpretation since it showed hypoacidity more often than not, occasionally complete anacidity of the stomach contents. Consequently hydrochloric acid has been tried, effectively in some instances.

Whatever the benefits of either alkali or acid therapy, the composition of the gastric juice is not fundamentally at fault. Responsible for the ailment is temporary impairment of the neuromuscular mechanism which controls transportation of the gastric contents.

During pregnancy, the position and motility of the stomach delay the emptying time of this organ, and favor the development of reverse currents that carry material upward. It may reach the esophageal mucous membrane, stimulate contraction of the cardiac sphincter and thus cause heartburn.

With a few exceptions, the hypodermic administration of prostigmin has given relief usually for several days at least. In the event the discomfort recurs this treatment may be repeated.

I wish to acknowledge my indebtedness to Dr. Richard Taylor, radiologist at the Hospital of the Good Samaritan, Los Angeles, California, for the fluoroscopic and x-ray work done in the preparation of this article.

REFERENCES

(1) *Barry, D. T.:* Irish J. M. Sc. 749, October, 1939. (2) *Schmidt, H. W.:* Am. J. Digest. Dis. **6**: 693, 1939. (3) *Evans, J. R., and Bouslog, J. S.:* Radiology **34**: 530, 1940. (4) *Hansen, Rolf:* Centralbl. f. Gynäk. **61**: 2306, 1937. (5) *Winter, E. W.:* Centralbl. f. Gynäk. **58**: 443, 1934. (6) *Winkler, H.:* Monatschr. f. Geburtsh. u. Gynäk. **100**: 125, 1935. (7) *Mason, L. W.:* Colorado M. J. **28**: 392, 1931. (8) *Rodway, Helen E., and Shelley, Orsula:* J. Obst. & Gynaec. Brit. Emp. **42**: 107, 1935. (9) *Brian, Raynor S.:* Brit. M. J. **2**: 970, 1933. (10) *Strauss, M. B., and Castle, Wm. B.:* Am. J. M. Sc. **184**: 655, 1932. (11) *Mann and*

Mann: Am. J. Digest. Dis. **6:** 322, 1939. (12) *Morrison, S., and Feldman, M.:* Am. J. Digest. Dis. **6:** 549, 1939. (13) *Polley, Howard F.:* J. A. M. A. **116:** 821, 1941. (14) *Slemons, J. M.:* West. J. Surg. **48:** 7, 1940. (15) *Mancini:* Chem. Abstract **28:** 7362, 1934. (16) *Cannon and Rosenblueth:* Am. J. Physiol. **119:** 285, 1937. (17) *Dale, Sir Henry:* Chemical Transmission of the Effects of Impulses in the Peripheral Nervous System, Lilly Research Laboratory Dedication, 1935. (18) *Jones, Chester M.:* Digestive Tract Pain, New York, 1938, The Macmillan Company.

409 NORTH CAMDEN DRIVE

DISCUSSION

DR. ALEXANDER M. CAMPBELL, GRAND RAPIDS, MICH.—Dr. Williams' statement that the hydrochloric acid in the gastric juice is markedly reduced has been verified by different research workers, but the fact as yet does not seem to be generally recognized by obstetricians. Rodney and Shelley of London investigated 100 cases of heartburn and in only 11 per cent was there a high volume of hydrochloric acid. Yet hyperchlorhydria has usually been considered as the basic cause of heartburn.

The question arises as to what produces the hypochlorhydria of pregnancy, and the relation it has, if any, to heartburn? Castle and Strauss show that in the physiologic anemia of pregnancy, over 50 per cent have a decrease or absence of hydrochloric acid, and that there is a return to normal following parturition. It is estimated that about 50 per cent of pregnant women suffer from a pathologic anemia which suggests that this condition plays a role in the etiology of heartburn.

Sandweiss and his collaborators report that in over 70,000 consecutive admissions of pregnant women to five Detroit Hospitals during a ten-year period, there was only one active case of peptic ulcer, and they suggest that the improvement observed in ulcer during pregnancy may be related to the large amount of A.P.L. hormone present at that time.

Dr. Williams' paper suggests more study of this syndrome which may clarify its etiology and place its management on a scientific basis. It would be of special interest if he continued his research with the dilating balloon to observe what effect prostigmin has on gastric motility in cases of heartburn during pregnancy.

From a long clinical experience in the management of the parturient woman I am of the opinion that in heartburn the neurogenic factor is extremely important and that by a sympathetic, intelligent and painstaking attempt to evaluate all emotional disturbances and all environmental, domestic, and financial maladjustments that much can be done to prevent this disagreeable complication. Until sufficient research work is done to establish the etiologic factors, one can accomplish a great deal by suggestive therapy and a well-balanced liberal diet.

DR. M. PIERCE RUCKER, RICHMOND, VA.—The title of Dr. Williams' paper has been well chosen. Not only has he given us a clinical study of heartburn, but also a very timely study of the physiology of the stomach during pregnancy. Few such studies have been made. Hansen in 1937 showed that toward the end of pregnancy the position of the stomach was markedly changed. It was pushed up into the left dome of the diaphragm, and was rotated some 45 degrees until it lay as a flaccid bag more or less horizontally, on the top of the fundus of the uterus. The tone of the stomach was so much diminished that the emptying time was definitely increased. He did not think that the so-called anemia of pregnancy had anything to do with these changes. One might suppose that progestin might be the cause of the lessened activity of the stomach, but the recent work of Sleeth and VanLiere would seem to indicate that this hormone has no effect on the emptying time of the stomach.

Not only Hansen but others have shown that there is a tendency to hypoactivity during pregnancy. Dr. Williams has confirmed the findings of Hansen regarding the change in position and tone of the stomach. Any irritation, chemical or mechanical, of the lower end of the esophagus will cause heartburn.

As to the clinical aspects of the presentation, heartburn has not been as impressive a symptom with me as it evidently has been with Dr. Williams. In order to check this, I took at random from my files a number of antepartum records of

white, private patients. I was able to examine 408 of these carefully for a history of heartburn. I might say that while I ask routinely about nausea, gas, shortness of breath and palpitation of the heart, I do not have heartburn on my questionnaire. Twenty-six of these 408 patients complained of heartburn, or 6.37 per cent. The time in the pregnancy when this complaint occurred was as follows:

Third month	1	Seventh month	5
Fourth month	4	Eighth month	5
Fifth month	3	Ninth month	5
Sixth month	2	Tenth month	1

Since it is possible that those who aborted early or those who were seen only when they came into the hospital for delivery regarded heartburn as too trifling to mention a somewhat false idea of the frequency of this symptom might result. When I selected only those whose course I had personally followed for at least two months, there were 290 patients, 24 of whom complained of heartburn, a percentage of 8.3.

As to the relationship of heartburn to subsequently developing toxemia, my cases showed no serious toxemia. Seven had a systolic blood pressure of as much as 150 on at least one occasion, and two of these showed a trace of albumin in the urine.

The treatment that Dr. Williams suggests, i.e., with prostigmin, seems to me to be a logical one.

ROENTGEN PELVIMETRIC ANALYSIS OF WALCHER'S POSITION*

HAROLD M. BRILL, M.D., AND GERHARD DANELIUS, M.D., CHICAGO, ILL.
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THE Walcher position of extreme body hyperextension during labor is recommended in leading textbooks of obstetrics as a useful procedure in aiding the entrance of the fetal head into a moderately narrowed pelvis. Although critical reviews of this procedure have appeared periodically, and most of them have been in accord with Walcher's idea, several experienced obstetricians have voiced contrary opinions.

Even before Walcher's original publication in 1889,[30] Albucasis[6] in 1060 recommended a similar hanging position, as did also Mercurio[6] in 1589 and Melli[6] in 1738. In his original publication, Walcher reported the use of the hyperextended position in 6 patients, in all of whom were noted an increase in length of the diagonal conjugate of from 8 to 13 mm. No additional data were presented in his subsequent presentation ten years later.[31] Since then, a considerable number of reports have appeared and these have been exhaustively reviewed by Jarcho[15] in 1929.

Many authors, including Duehrssen,[9] Kalt,[16] Fehling,[10] Fothergill,[11] Krukenberg,[6] Jarcho[15] and others,[3, 5, 7, 8] have concurred in Walcher's original contention that this position causes a definite increase in the diagonal conjugate, and is therefore, a beneficial procedure. Apparently, all of these authors measured the increase of the diagonal conjugate from the hyperflexed (exaggerated lithotomy position) to the hyperextended (Walcher) position as did Walcher originally.

The present-day textbook opinion is presented as follows: DeLee[6] recommends, as one method of treatment for a moderately contracted pelvis, the use of the Walcher position "in which can be obtained a lengthening of the conjugate of from six to twelve millimeters." Interestingly enough, he also states that he has "curiously obtained as good or better results with the exaggerated lithotomy position." Sellheim,[21] in Halban-Seitz's handbook, states that "in Walcher's position . . . the inlet will be widened in the straight diameter, the outlet narrowed." Titus[28] feels that "additional space may be given during delivery while the head is above the midpelvis with the Walcher position." Williams[33] also teaches that in "contracted pelves with a conjugate vera of from nine to ten centimeters, if engagement fails to occur after complete dilatation of the cervix, the patient should be placed in the Walcher position. In many cases, this procedure will bring about a sufficient lengthening of the anteroposterior diameter of the superior strait to permit engagement."

*Read at a meeting of the Chicago Gynecological Society, May 16, 1941.

In our opinion, the problem is a twofold one: First, is the Walcher position of such established efficiency as to warrant its use in spite of the great distress that it causes the laboring woman; and second, if this efficiency is conceded, is the accepted explanation correct, namely, that an *increase* in the length of the obstetric conjugate is produced?

Walcher originally contended that because of a rotatory movement of the iliac bones against the sacral bone around a transverse axis, the distance from the moving symphysis to the stationary sacral promontory could be increased from 0.8 to 1.3 cm. This statement can easily and accurately be checked by modern roentgen pelvimetry as was suggested by Jarcho[15] eleven years ago.

Concerning the theory and the mechanics of Walcher's position, the accepted explanation is that the weight of both legs hanging downward unsupported, pulls on the pelvic ring and produces the maximum possible downward rotation of its anterior half. The sacrum and its promontory, however, are fixed in their position by the counter pull of the spine. These movements in the sacroiliac articulations are favored by the softening of the ligaments which accompanies pregnancy. The exact location of the transverse axis of the rotatory movement has been determined by anatomists[17] as below and posterior to the promontory.

One grave criticism can be levelled against Walcher's conception. Walcher and many of his subsequent supporters measured the diagonal conjugate in the extreme exaggerated lithotomy position "by drawing the knees up as high as possible toward the body," and in the extreme hyperextended position thus comparing the two extremes. Since the purpose of Walcher's position is to facilitate the entrance of the fetal head into the inlet, thus indicating its use during the first and second stage of labor, it is obvious that the extreme lithotomy position need not be considered here, and that logical comparison should be made between the ordinary comfortable dorsal position and the Walcher position. This criticism was first expressed in 1891 by Klein,[17] who proved in his study on cadavers that the *decrease* in the length of the conjugate from the dorsal to the extreme lithotomy position far exceeded the *increase* in the length of the conjugate from the dorsal to the hanging position. This increase was as little as 0.1 cm. in normal, 0.05 cm. in large, and 0.07 cm. in contracted pelves.

Another criticism based upon some fundamental principles in Walcher's position was made by Wahl[29] in 1930, who emphasized the fact that the axis for the sacroiliac rotatory movement is located *below* and posterior to the sacral promontory. Some contracted pelves present a prominent promontory with a pronounced sacral excavation. In this group, a downward rotation of the symphysis will theoretically produce some enlargement of the obstetric conjugate. A fairly large group of contracted pelves, however, show a straight, flat sacrum with a prominence at the junction of the first and second sacral vertebras or lower down. The functioning obstetric conjugate in these cases should be plotted from the symphysis to this sacral prominence rather than to the anatomical promontory. Since this prominence is located below the transverse axis of rotation, a downward tilting of the symphysis will theoretically *shorten* rather than *lengthen* the obstetric conjugate, thus con-

traindicating the use of the Walcher position. In such cases, an upward rotation of the anterior half of the pelvic ring as obtained in the lithotomy position will theoretically *lengthen* the functioning conjugate (Figs. 9 and 10). This fact may explain DeLee's statement that

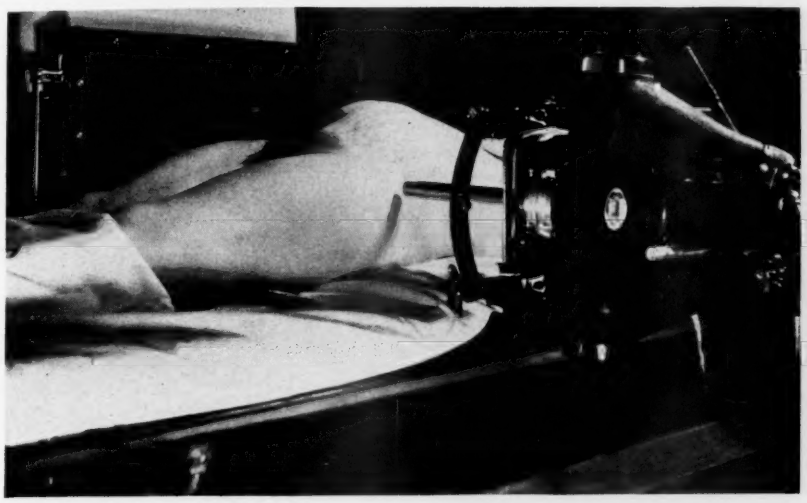


Fig. 1.

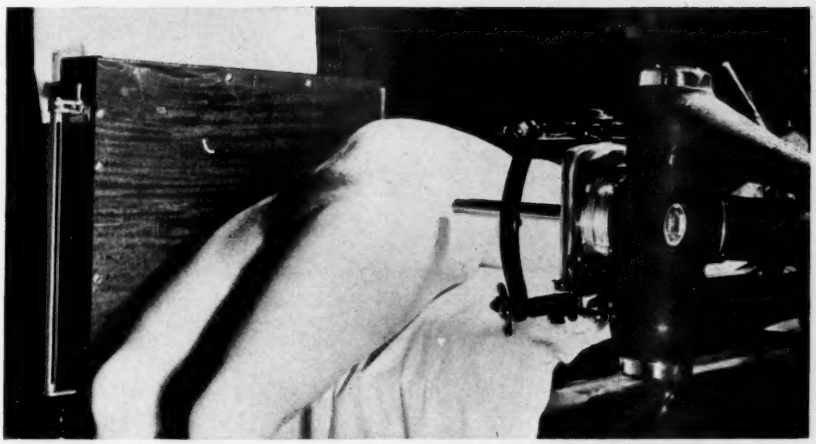


Fig. 2.

Figs. 1 and 2.—Technical setup for taking successive radiographs in dorsal and in Walcher's positions.

he "curiously obtained as good or better results with the exaggerated lithotomy position which is theoretically contraindicated because it is supposed to contract the anteroposterior diameter of the inlet." Wahl,[29] however, did not support his ideas with the use of roentgen pelvimetry.

PRESENT STUDY

To obtain the best comparative roentgenographic measurements of the pelvis, we chose a method which reduced to a minimum any changes

in the technical arrangements and the positioning of the patient. All exposures, therefore, were made with the patient in a supine position in order to exclude any possible influence resulting from rotating the patient laterally. In addition, this arrangement permitted the position of the cassette holder, the tube-stand, and the target film distance to remain unchanged.

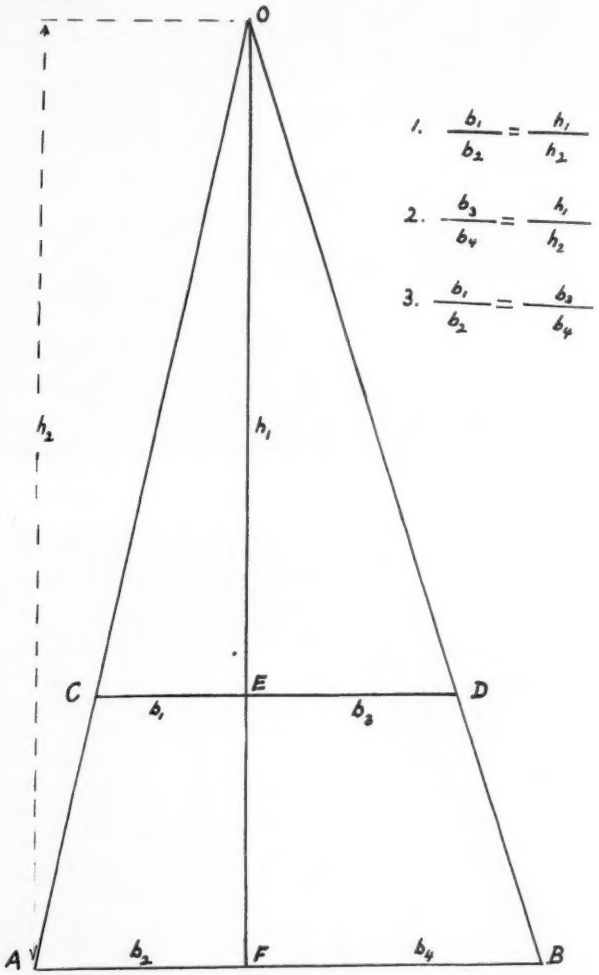


Fig. 3.—Diagram illustrating Euclid's geometrical theorem of the similar triangles in which the altitudes are proportional to their bases.

The patient was placed horizontally in the dorsal position on a cart in front of an upright Potter-Bucky grid with the pelvis directly over the center of the film. The x-ray beam leaving the target horizontally, was directed transversely through the pelvis (Fig. 1). Following the first exposure, the tube stand and Potter-Bucky grid remained unchanged, while the cart was advanced to a point where its caudal edge was approximately at the vertical center line of the Potter-Bucky grid. The patient was then placed in the Walcher position over the edge of the cart and properly centered for the second exposure (Fig. 2). With

this technique any minor errors would be equally apparent on both films, and therefore, direct, accurate comparison could be made.

To obtain the actual measurements, a 10 cm. metal ruler was placed lengthwise over the lower abdomen of the patient directly over the midline, carefully avoiding any lateral tilting. The shadowgraph of

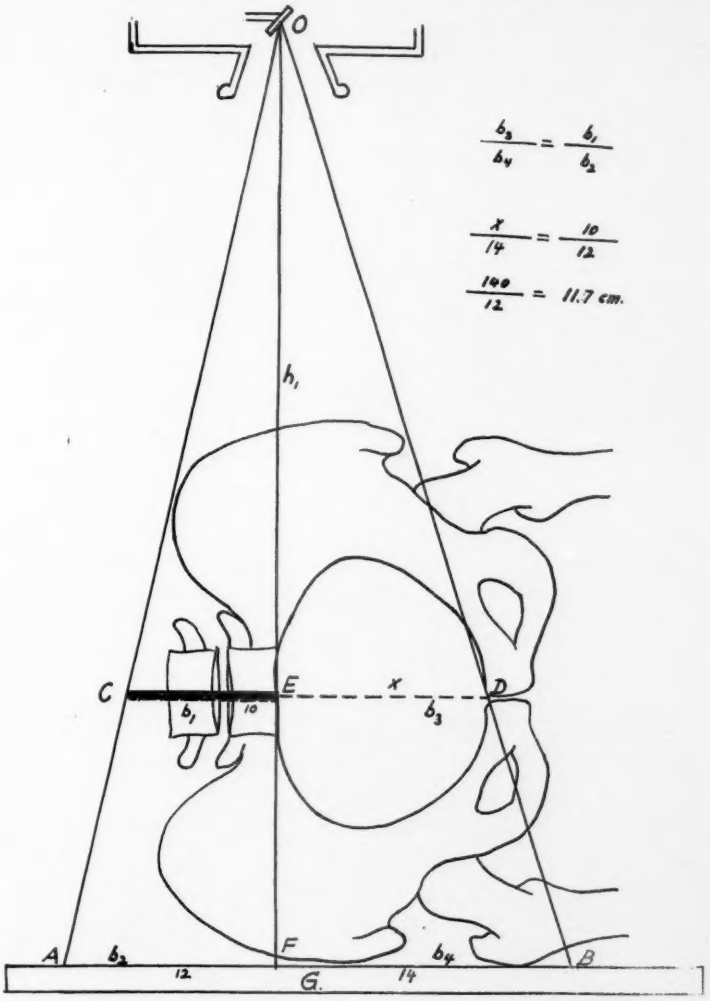


Fig. 4.—Bony pelvis, x-ray tube, film cassette (*G*), and a metal ruler (*C-E*) are transposed upon the previous diagram of the similar triangles. The simple equation shown herein may now apply.

the ruler on the film indicated the exact rate of enlargement on each radiograph (Fig. 6). This enlargement is an unavoidable by-product of the central projection in radiographic work.

The underlying principle of this method is based on the geometrical theorem of the "similar triangles" postulated by Euclid, in which the altitudes of two similar triangles are proportional to their bases. In this method of roentgenographic pelvimetry, two pairs of similar tri-

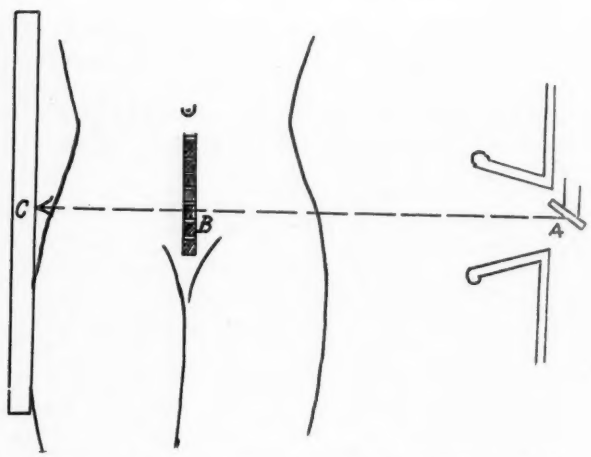


Fig. 5.—Illustrates the simplicity of the process of centration and placement of the metal ruler (*B*) in the "metal rod method" of roentgen pelvimetry.

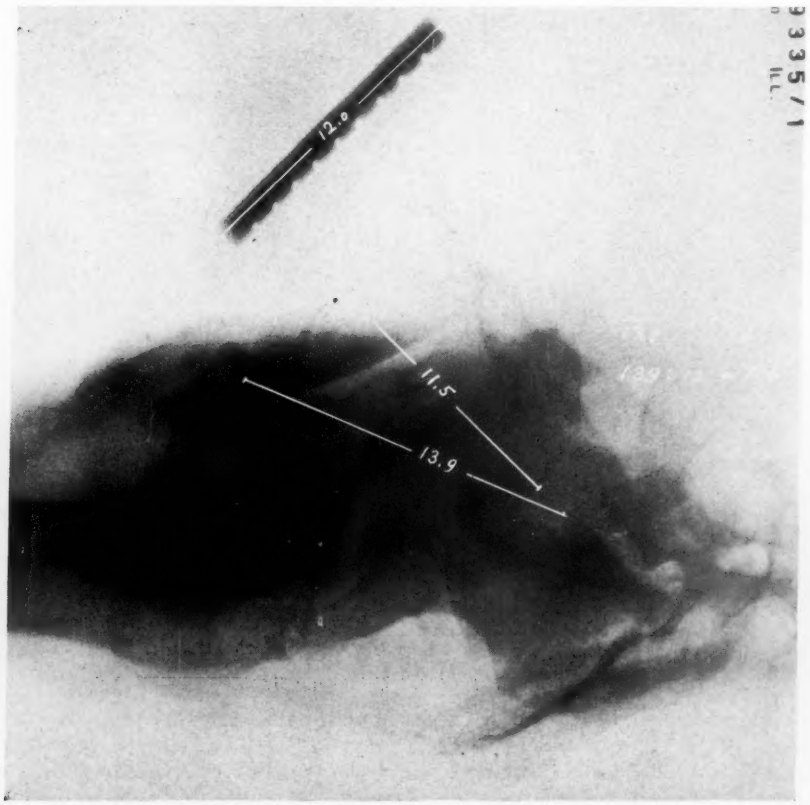
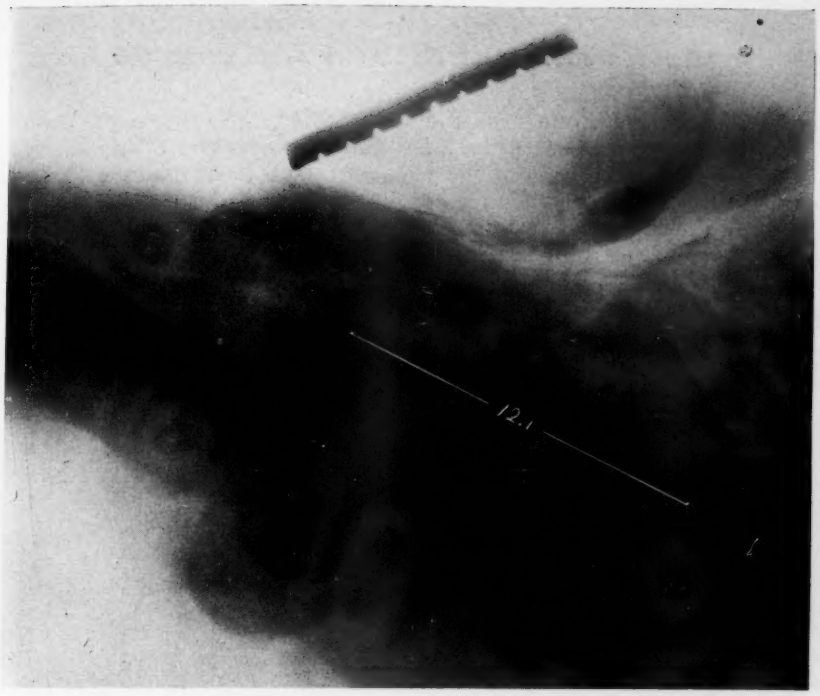
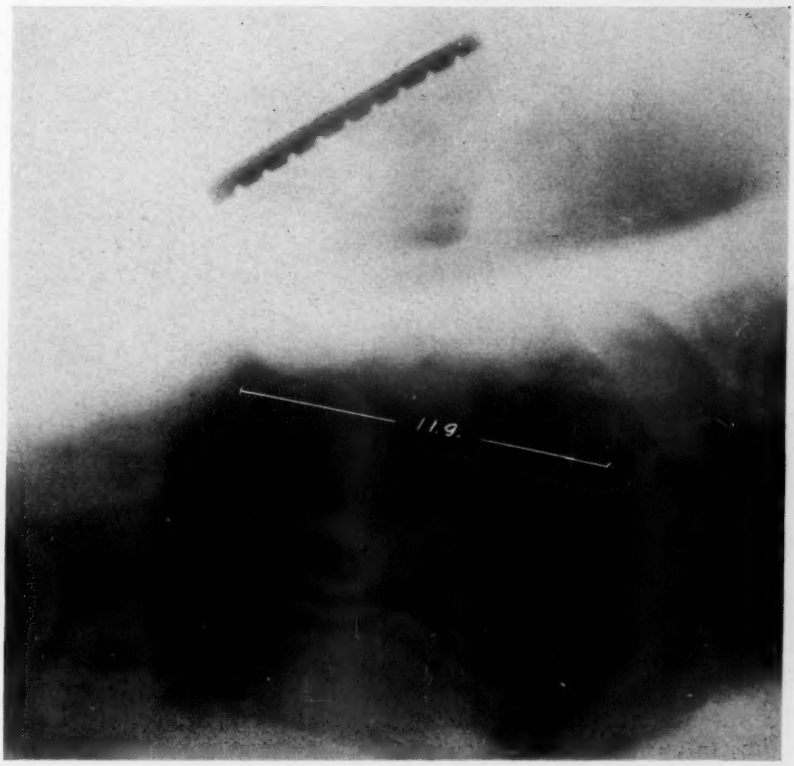


Fig. 6.—Radiogram with pertinent measurements inserted. The equation is $\frac{x}{13.9} - \frac{10}{12}$, $12X = 139$, $X = 11.6$. The obstetric conjugate measures 11.6 cm. as calculated herein.



A.



B.

Fig. 7.—Pair of radiograms taken in the slightly flexed (*A*) and Walcher (*B*) positions demonstrating that comparison and measurement can be accurately performed. The conjugate in the dorsal position equals 12.1 cm. and in Walcher position 11.9 cm. The result is a *decrease* of 0.2 cm.

angles are obtained, one with the metal ruler, the other with the obstetric conjugate as the easily identifiable base (Figs. 3 and 4). The first essential condition for the production of these pairs of similar triangles is that their altitudes be exactly identical, and this requires that both the metal ruler and obstetric conjugate be placed at exactly the same distance from the film and target. This is accurately accomplished by placing the ruler over the midline of the patient while lying on her back (Fig. 5). Thus, the metal ruler and the obstetric conjugate

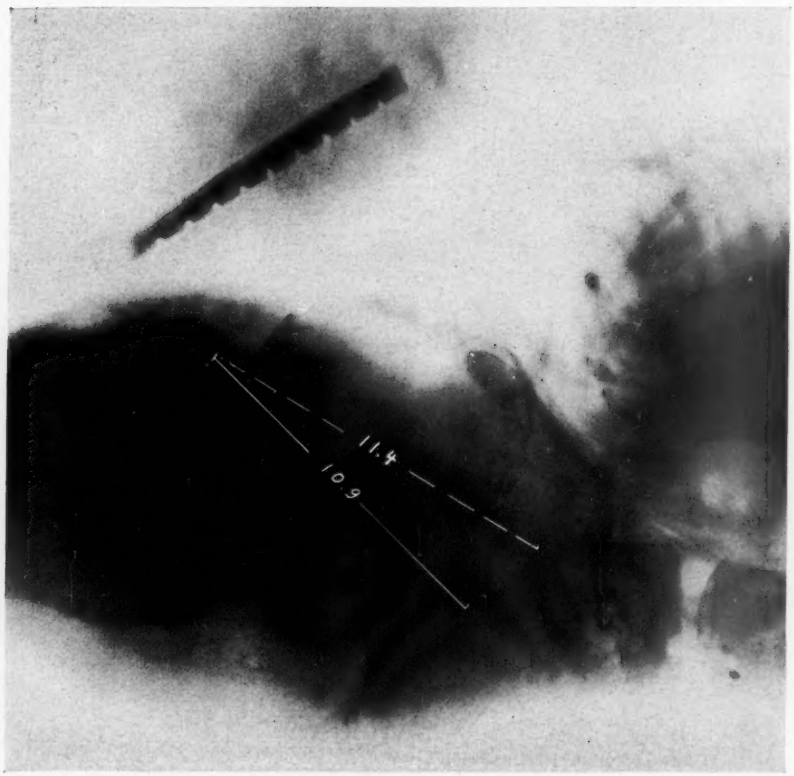


Fig. 8-A.

Fig. 8.—A pair of radiograms illustrating a transition type of pelvis with a promontory and a sacral prominence below it. Here the functioning conjugate must be plotted to this sacral prominence. Walcher's position *decreases* the length of the functioning (lower) conjugate by 0.2 cm. while not affecting the (upper) conjugate.

are equidistant from the film. The second condition demands that the base lines be exactly parallel. This, too, is easily secured by careful centration and by avoiding any such tilting of the ruler which would bring one end closer to the film than the other. By this method, the measurement of the obstetric conjugate is proved to be reliable within a range of approximately ± 0.2 cm.[13, 18, 24]

Representative illustrations from our study are inserted below to demonstrate the essential features of our investigation.

Fig. 6 is a lateral view of the pelvis measured by the metal rod method with the actual measurements and pertinent equation thereon.

Fig. 7 is a comparative study of the pelvic inlet in the moderately flexed (*A*) and the Walcher (*B*) position, demonstrating a shortening of 0.2 cm. in the true obstetric conjugate in Walcher's position.

Fig. 8 is a comparative study of a transition type of pelvis in the dorsal (*A*) and the Walcher (*B*) positions. There is present an anterior sacral prominence at the junction of the first and second sacral segments. Here the functioning obstetric conjugate must be plotted from the symphysis to this anterior sacral prominence rather than to the anatomic promontory. Measurements of both conjugates are inserted for comparison and show that the functioning conjugate is 0.5 cm. and

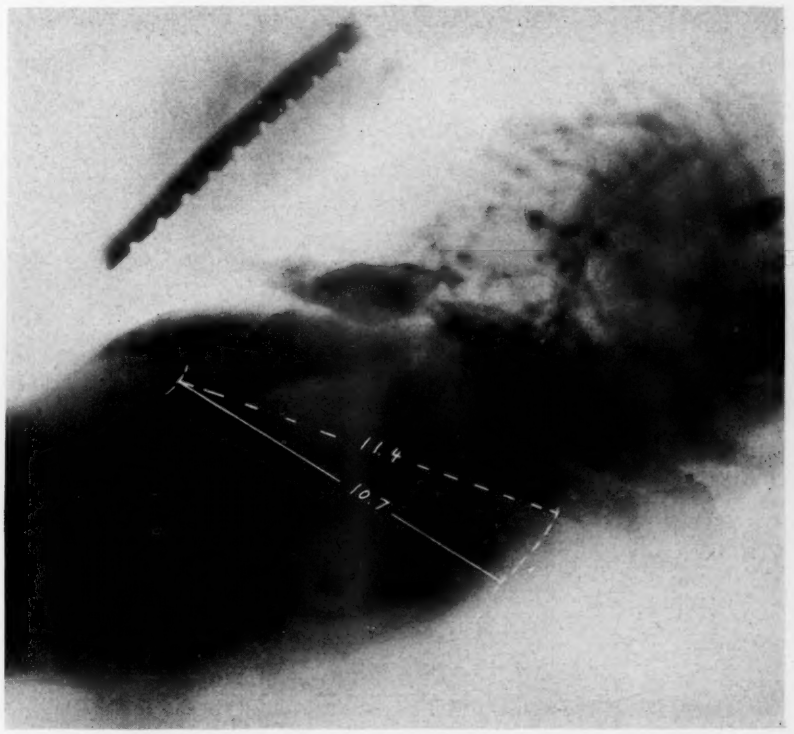


Fig. 8-*B*.

0.7 cm., respectively, shorter than the anatomic conjugate in both positions. Walcher's position (*B*) causes a shortening of 0.2 cm. in the functioning conjugate while the anatomical conjugate is unaffected.

Fig. 9 shows another transition type of pelvis with a marked anterior sacral prominence.

Fig. 10 is a superimposed tracing of this pelvis with several geometrically determined hypothetical positions of the symphysis inserted. *D* is the normal symphyseal position as traced directly from the x-ray film. Again, the functioning conjugate must be plotted to the anterior border of the sacrum (P_2) while "routine" (thoughtless) plotting to the anatomical promontory (P_1) would result in a measurement 1.1 cm. in excess of the correct length (9.8 cm. as against 10.9 cm.).

The transverse axis of rotation of the anterior pelvic ring, in the sacroiliac junctions, the key principle of Walcher's theory, has been

located by anatomists at a point posterior to and below the promontory (*A*). Using *A* as the *center of rotation,* the theoretical position of the symphysis in Walcher's position (*W*), and in lithotomy position (*L*) was *geometrically determined.* These determined positions result in a shortening of the conjugate of 0.3 cm. in Walcher's position (*W*) but in a lengthening of 0.5 cm. in lithotomy position (*L*). Thus do we find the theoretical foundation of DeLee's clinical observation that in

Fig. 9.

Figs. 9 and 10.—X-ray film and diagram of this film in which the functioning conjugate must be plotted to such an anterior sacral prominence (P_2) as was shown in the previous illustration. Geometrically, the positions of the symphysis in the lithotomy (*L*) and Walcher (*W*) positions are determined. Again Walcher's position *shortens* the functioning conjugate (9.5 cm.) while the lithotomy position considerably *lengthens* it (10.3 cm.), thus contraindicating Walcher's position.

some cases he "curiously observed as good or better results with the exaggerated lithotomy position." The above described pelvis represents a group wherein Walcher's posture is contraindicated during the conduct of labor, while lithotomy position may have a beneficial effect.

Fig. 11 shows a similar geometrical determination for dorsal (*D*) and lithotomy (*L*) position in a *normal profile pelvis* with a good sacral excavation. Here lithotomy position brings about a definite shortening of the conjugate (0.7 cm.) compared with its original length in the comfortable dorsal position. This shortening of 0.7 cm. represents the increase in length of the obstetric conjugate which Walcher erroneously claimed for his posture. By comparing his posture to the lithotomy position instead of to the dorsal position, Walcher shortened the conjugate and then recovered this loss.

In our series twenty patients were studied, ten in labor and ten during gestation. Seven of each group were x-rayed in the comfortable dorsal position, and the remaining three in the moderately flexed position. In each patient comparative measurements were made with the Walcher position. Attempts to measure the conjugate in the exaggerated lithotomy position have, thus far, been unsuccessful. Tables I, II, and III illustrate the details.

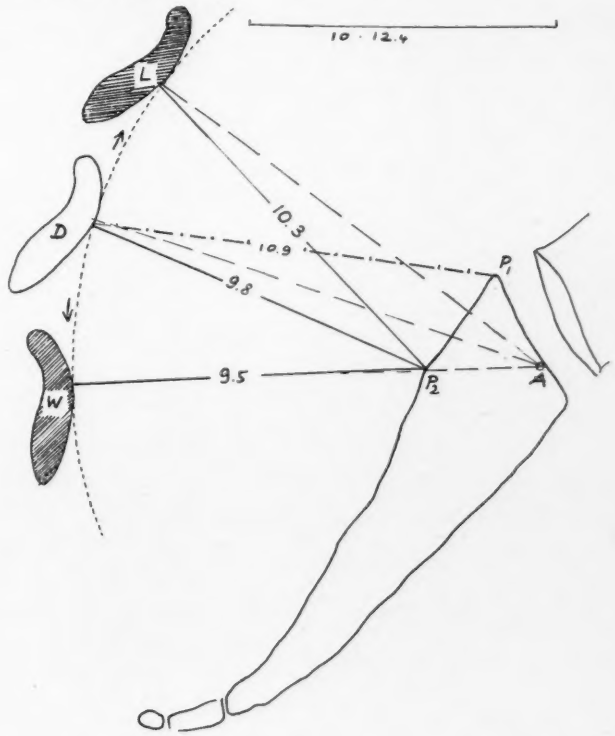


Fig. 10.

DISCUSSION

These results would indicate, that, in the average, the length of the obstetric conjugate, comparing the comfortable dorsal with Walcher's position, shows a negligible change of about 0.25 cm. Shortening occurs twice as frequently as lengthening. However, when comparing the moderately flexed position with Walcher's position an only apparent increase in the length of the obstetric conjugate averaging about 0.4 cm. is observed. This apparent lengthening actually is only the recovery of the original *shortening* of the obstetric conjugate which shortening was artificially produced through the change from the comfortable dorsal to the lithotomy position.

In none of our cases, comparing the various positions, did we even approach as great an increase in the obstetric conjugate "of from 0.8 to 1.3 cm." as claimed by Walcher.

Inasmuch as clinical observations of noted obstetricians for many years past have established the efficiency of the Walcher position, we

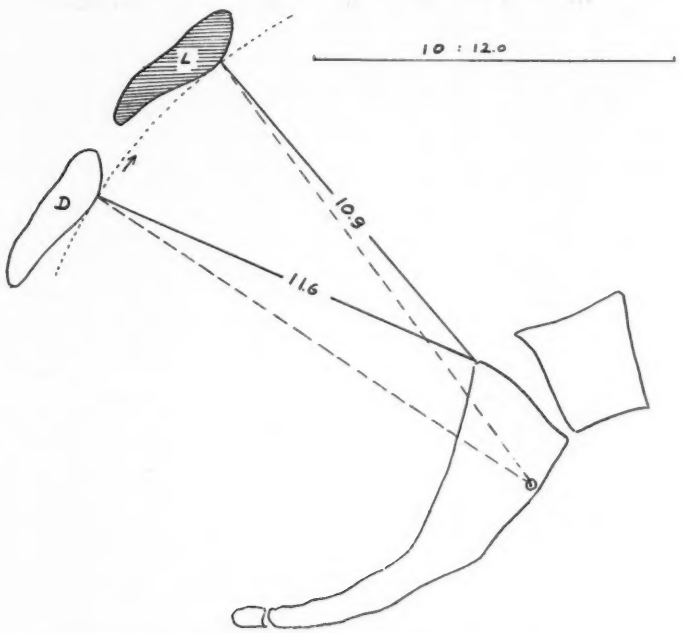


Fig. 11.—Diagram of a pelvis with a normal profile, demonstrating that the lithotomy position (*L*) *decreases* the length of the obstetric conjugate (10.9 cm.) as compared to its length of 11.6 cm. in comfortable dorsal position (*D*).

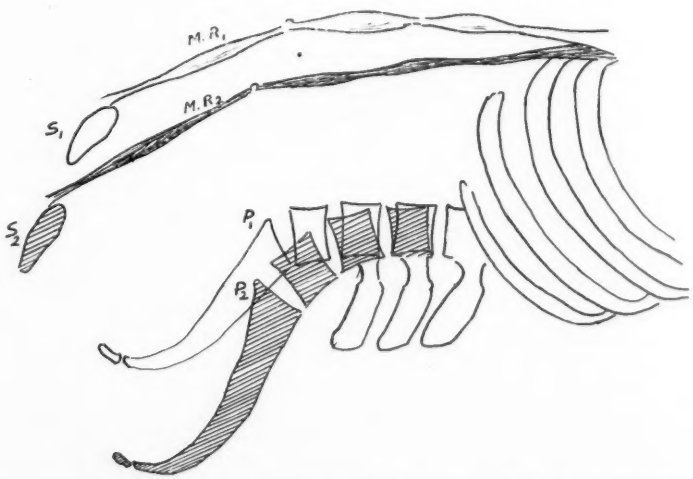


Fig. 12.—Demonstration of our theory concerning the efficiency of Walcher's position. Cross section through a pelvis, lumbar spine and abdominal rectus muscles in dorsal and in Walcher's positions (shaded). The distance from the origin to the insertion of the rectus muscles ($M.R_1$ and $M.R_2$) is materially increased in Walcher's posture and greatly increases the power of the auxiliary abdominal musculature (Bauchpresse). We also note the change in the angle of inclination of the pelvic inlet. Both factors may facilitate the entrance of the fetal head into the pelvis.

TABLE I. STUDIES DURING PREGNANCY

CLINICAL DATA	OBSTETRIC CONJUGATE		SPECIAL FEATURES	DIFFERENCE CM.
	DORSAL	WALCHER		
Comparison of comfortable dorsal with Walcher's position				
1. L. C., para iii 32 weeks	11.0	11.0		±0
2. A. D., para i 30 weeks	12.0	12.2		+0.2
3. F. R., para i 32 weeks	13.7	13.6		−0.1
4. L. S., para ii 25 weeks	13.3	12.9	Flat sacrum	−0.4
5. S. C., para ii 30 weeks	11.9	12.3		+0.4
6. L. A., para iii 36 weeks	11.9	11.8		−0.1
7. A. S., para i 30 weeks	12.5	12.4		−0.1
7 cases		Increase 2	Average	+0.3 cm.
		No change 1	Average	0 cm.
		Decrease 4	Average	−0.2 cm.
Comparison of moderately flexed with Walcher's position				
1. S. L., para ii 27 weeks	12.1	11.9		−0.2
2. J. S., para ii 25 weeks	11.9	12.1		+0.2
3. L. L., para i at term	11.5	12.0		+0.5
3 cases		Increase 2	Average	+0.35 cm.
		Decrease 1	Average	−0.2 cm.

TABLE II. STUDIES IN LABOR

CLINICAL DATA	OBSTETRIC CONJUGATE		SPECIAL FEATURES	DIFFERENCE CM.
	DORSAL	WALCHER		
Comparison of comfortable dorsal with Walcher's position				
1. C. Z., para i 2nd stage, +1, 8 cm.	10.7	10.7		0
2. A. R., para i 2nd stage, +1, 6 cm.	11.9	12.1		+0.2
3. M. S., para i 2nd stage, +2, 8 cm.	11.7	11.3	Assimilation pelvis	−0.4
4. I. P., para i 2nd stage, +2 complete	11.7	12.3		+0.6
5. M. D., para i 1st stage, 0, 6 cm.	13.4	13.3		−0.1
6. S. G., para i	11.4	11.4	Prominent first	0
1st stage, 0, 3 cm.	10.9	10.7	sacral disc	−0.2
7. R. B., para i 1st stage, −1, 4 cm.	12.1	12.0		−0.1
7 cases		Increase 2	Average	+0.4 cm.
		No change 1	Average	0 cm.
		Decrease 4	Average	−0.2 cm.
Comparison of moderately flexed with Walcher's position				
1. S. S., para i 1st stage, −2, 2 cm.	13.2	13.5		+0.3
2. B. T., para i 2nd stage, +1, 8 cm.	10.2	10.4		+0.2
3. B. S., para i 2nd stage, +1, 6 cm.	11.0	11.8	Marked flexion of thighs	+0.8
3 cases		Increase 3	Average	+0.43 cm.

TABLE III.

NUMBER OF CASES	INCREASE	DECREASE	UNCHANGED
Comparison of all cases of dorsal and Walcher's position			
14	4, average + 0.35 cm.	8, average - 0.2 cm.	2
Comparison of all cases of flexed and Walcher's position			
6	5, average + 0.4 cm.	1, average - 0.2 cm.	0

must therefore search for the true causes of such beneficial effects, disregarding any lengthening of the conjugate. We offer the following as possible explanations. The angle of inclination of the pelvic inlet is considerably altered (Jarcho, Jacobs) in Walcher's position, through, we believe, increased lordosis of the lumbar spine, and thus may facilitate the entrance of the fetal head. Furthermore, there results a considerable increase in distance from the origin to the insertion of the rectus muscles (Fig. 12) in Walcher's posture.

According to an important law of muscular physiology,[23] the power of a muscle is greatly increased as its tension at rest increases and vice versa. Consequently the power of the auxiliary abdominal muscular apparatus (Bauchpresse) is greatly increased in Walcher's posture and may also act as a lever to guide the head into the inlet.

Further roentgenographic studies are indicated concerning the behavior of the lower lumbar spine and lumbosacral junction, and the behavior of the fetal head in Walcher's posture. All these studies may ultimately lead to the discovery of a procedure less distressing to the patient yet preserving the clinical advantages claimed for Walcher's position.

CONCLUSIONS

1. As compared to the comfortable dorsal position, Walcher's position does not *increase* the length of the obstetric conjugate, in a normal, profiled pelvis.

2. As compared to the comfortable dorsal position, the exaggerated lithotomy position *decreases* the length of the obstetric conjugate, in a normal profiled pelvis.

3. The *shortening* of the obstetric conjugate in the exaggerated lithotomy position led Walcher to the erroneous conclusion that the conjugate is *lengthened* in the position he advocated.

4. In difficult breech extraction, in a normal profiled sacrum, it is deemed advisable to change from lithotomy to Walcher position for delivery of the shoulders and aftercoming head, because the artificially *shortened* conjugate will thus recover its loss.

5. In flat sacrum pelves with an anterior sacral prominence, Walcher's position is contraindicated, while lithotomy position will give additional space at the inlet.

6. The two factors of increased muscular tension and altered angle of inclination may explain the reputed clinical efficiency of Walcher's position.

7. Theoretically, a device such as a low abdominal pressure-band and an elevation of the lumbar spine to a moderate lordosis may produce the advantages claimed by Walcher in a far less distressing manner to the patient.

We wish to express our gratitude to Dr. Aaron E. Kanter, chief of the first Gynecological Service of the Mount Sinai Hospital, for his generous aid and kind suggestions in the preparation of this study.

REFERENCES

(1) *Bell, J. W.:* Am. J. Obst. & Gynec. **2:** 616, 1921. (2) *Chamberlain, W. E.:* Am. J. Roentgenol. **24:** 621, 1930. (3) *Christiani, J.:* Wien. klin. Rundschau. **27:** 499, 465, 485, 1913. (4) *Coats, A. J.:* Northwest Med. **26:** 542, 1927. (5) *Cutts, R. E.:* Ann. Gynaec. & Pediat. **13:** 594, 1899-1900. (6) *DeLee, J. B.:* The Principles and Practice of Obstetrics, ed. 7, Philadelphia, 1938, W. B. Saunders Co., p. 809. (7) *Dice, W.:* Am. J. Obst. **63:** 459, 1911. (8) *Dickinson, R. L.:* Am. J. Obst., N. Y. **39:** 751, 1899. (9) *Duehrssen:* Gesellsch. f. Gynäk. **5:** 46, 1893. (10) *Fehling, H.:* Muenchen. med. Wchnschr **41:** 861, 1894. (11) *Fothergill, W. E.:* Brit. M. J. **2:** 1290, 1896. (12) *Goldthwaite, Joel E., and Osgood, R. B.:* Boston M. & S. J. **152:** 593, 1905. (13) *Guthmann, H.:* Arch. f. Gynäk. **133:** 415, 1928. (14) *Jacobs, J. B.:* Am. J. Obst. & Gynec. **15:** 689, 1928. (15) *Jarcho, Julius:* Surg., Gynec. & Obst. **49:** 854, 1929. (16) *Kalt, A.:* Cor.-Bl. f. Schweiz. Aerzte. **24:** 652, 1894. (17) *Klein, G.:* Ztschr. f. Geburtsh. u. Gynäk. **21:** 74, 1891. (18) *Liepman, W., and Danelius, G.:* Geburtsh. u. Roentgenbild. p. 171, 1932. (19) *Litzenberg, J. C.:* J. A. M. A. **69:** 1759, 1917. (20) *Lynch, F. W.:* Surg., Gynec. & Obst. **30:** 575, 1920. (21) *Sellheim, H.:* Halban Seitz, Biologie u. Pathologie des Weibes, vii, 1, 102. (22) *Spencer, H.:* Lancet **1:** 1568, 1912. (23) *Steindler, A.:* Mechanics of Normal and Pathological Locomotion in Man, Charles C Thomas, 1935, pp. 76, 129. (24) *Thoms, H.:* J. A. M. A. **85:** 253, 1925. (25) *Idem:* Am. J. Surg. **47:** 691, 1940. (26) *Idem:* Am. J. Obst. & Gynec. **38:** 634, 1939. (27) *Idem:* Am. J. Roentgenol. **44:** 9, 1940. (28) *Titus, P.:* Management of Obstetrical Difficulties, ed. 1, St. Louis, 1937, The C. V. Mosby Co., p. 451. (29) *Wahl, F. A.:* Arch. f. Gynäk. **142:** 668, 1930. (30) *Walcher, G.:* Zentralbl. f. Gynäk. **51:** 892, 1889. (31) *Idem:* St. Louis Courier Med. **21:** 341, 1899. (32) *Wehl, E. J.:* Arch. f. Gynäk., Berl. **45:** 323, 1893-4. (33) *Williams, J. W.:* Obstetrics, ed. 5, New York, 1923, D. Appleton-Century Co., p. 865. (34) *Winter, G.:* Halban Seitz. Biologie u. Pathologie des Weibes, viii, 2, p. 231.

Sadusk, Jr., Waters, and Wilson: The Treatment of Anuria Due to Sulfapyridine Calculi, J. A. M. A. **115:** 1968, 1940.

The authors offer this report as a means of additional evidence that complete anuria due to sulfapyridine may be caused by ureteral obstruction and that this condition can be treated effectively by means of cystoscopy. The concretions may exist without blocking the ureters, and under these circumstances treatment of sulfapyridine hematuria by means of forced fluids alone seems ample, since data have been offered to suggest that the concretions may be redissolved or washed out. If complete anuria is present, cystoscopy and ureteral catheterization should be carried out, and the kidney pelvis should be thoroughly washed with warm water until urine drips from the catheter. This is followed by a retrograde pyelogram to outline the upper urinary tract. It is preferable to leave the catheters in for the next twelve hours and force fluids. Both acidity and alkalinity of the urine have been claimed as etiologic factors. Low urinary output has been advanced as an additional factor. The question of the sodium salt of sulfapyridine being more toxic than sulfapyridine itself as far as urinary symptoms are concerned is also discussed. Other pathologic changes in the upper urinary tract consist of tubular and capsular dilatation, marked congestion and vacuolization within the glomerular tufts, and an acute hemorrhagic pyeloureteritis extending into the adjacent renal medullary tissue.

William Berman

HEMORRHAGIC DIATHESIS OF THE NEWBORN

Effect of Vitamin K Prophylaxis and Therapy

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HEMORRHAGIC disease of the newborn has been recognized as a clinical entity for many years; for a complete discussion of the subject, the reader is referred to the excellent monograph of Salomonsen.[1] The prophylactic and curative effect of preparations having vitamin K activity has been demonstrated. A comprehensive survey by Brinkhous[2] contains most of the present knowledge concerning vitamin K.

The principal objective of our investigation was to evaluate the prophylactic effect of antenatal administration of menadione (2-methyl-1, 4-naphthoquinone[3]) to mothers; a few observations on treatment have also been made. The responsibility for the study was divided; one of us (W. E. P.) supervised the therapy of the mothers; another (H. S. McK.) examined the eye grounds of the infants; and the third (L. G. P.) made serial determinations of microprothrombin time in the babies and instituted treatment when necessary. Measurements of prothrombin time were not made on the mothers, as no constant correlation has been found[4-6] between the levels in mothers and their infants. Determinations of coagulation time were made on a relatively small number of the babies simultaneously with the prothrombin times.

The expectant mothers were divided into three categories. One group received menadione before delivery for periods varying from three days to six weeks; a second group was treated during labor; a third was given no medicinal vitamin K. A preparation of 2-methyl-1, 4-naphthoquinone in tablet form* was used.

TECHNIQUE OF DETERMINING PROTHROMBIN TIME

For the determination of prothrombin times a simple bedside method was used, based on a procedure suggested by Quick,[7] and incorporating features utilized by Ziffren and his associates[8] and by Kato.[9] Since the completion of this investigation the application of an almost identical method has been reported by Lawson.[10]

Thromboplastin is prepared from the fresh brain of a young rabbit by removing vessels and meninges, grinding in a mortar and extracting with cold acetone at least four times, then removing the excess acetone by filtration. The residue is dried in the incubator overnight at 37° C. The resulting powder will retain its potency for approximately a month if kept tightly stoppered in a refrigerator. In order to prepare the

*Proklot, Eli Lilly and Co.

suspension of thromboplastin for use in the test, 0.3 Gm. of the powder is thoroughly shaken with 5 c.c. of isotonic sodium chloride solution in a clean test tube, which is then placed in a water bath at 45° C. to 50° C. for from ten to fifteen minutes. The thromboplastic suspension is then ready for use; it may be employed for several days if kept in the refrigerator when not needed; its potency is checked daily by estimating the microprothrombin time of a healthy adult. Before use the suspension is shaken and allowed to settle; the turbid supernatant fluid is utilized. It should be allowed to come to room temperature before use.

The required apparatus includes several 0.1 c.c. pipettes, small glass rods, a stop watch, a porcelain spot plate, and a pointed knife blade. The test is made at the infant's bedside. The heel is cleaned with alcohol and an incision is made about 2 mm. long and approximately the same depth; the heel is then wiped vigorously with a dry sponge to stimulate the flow of blood. One-tenth cubic centimeter of blood is drawn up in a pipette; if that amount cannot be easily obtained as little as 0.05 c.c. can be used. The blood is immediately transferred to the spot plate, and an equal amount of thromboplastic suspension quickly added. Simultaneously the stop watch is started and the mixture is agitated with a small glass rod. Vigorous stirring is continued for five seconds, after which the rod is drawn slowly back and forth through the mixture to determine the end point, which is the time when the preparation gels. The watch is stopped at the instant clotting is perceived.

The time required for coagulation to occur is designated as the microprothrombin time. In over 90 per cent of the normal control determinations the microprothrombin time was between seventeen and twenty-six seconds. This represents a greater variation than that reported by Lawson,[10] due probably to less uniformity in our thromboplastic preparation. That this factor is the chief one is suggested by improved uniformity in a small number of determinations made more recently with a standardized preparation.*

The performance of the test is simple; repeated determinations can easily be made on the same infant; this is not feasible with the usual methods requiring venous blood. The general plan was to perform the test on the first, third, and seventh days of life, but this schedule was varied in individual cases.

OBSERVATIONS OF PROTHROMBIN TIME IN INFANTS

Curves showing the microprothrombin times of 32 normal full-term infants whose mothers received no vitamin K are seen in Fig. 1. In general there is a tendency toward prolongation on the second and third days with a gradual return to normal after that time, but there are marked individual variations; several babies showed extreme prolongation on the first day. Two of these infants bled abnormally; a third had a cephalhematoma; the prothrombin times of all three responded promptly to vitamin K in oil,† given by mouth in two cases and in one case intramuscularly. In the two babies with external bleeding, the hemorrhage stopped within two hours after treatment; it was difficult to evaluate the effect on the cephalhematoma, although no further enlargement was noted.

*Bacto-Thromboplastin (from rabbit brain), Difco Laboratories, Detroit, Michigan.
†Thyloquinone (2-methyl-1, 4-naphthoquinone) in oil, Squibb.

The effect of administering menadione to the mother may be seen by referring to Figs. 2 and 3. Fig. 2 shows the microprothrombin curves of 54 infants of mothers treated during labor. Fig. 3 presents similar curves of 25 infants of mothers treated before labor. There is no de-

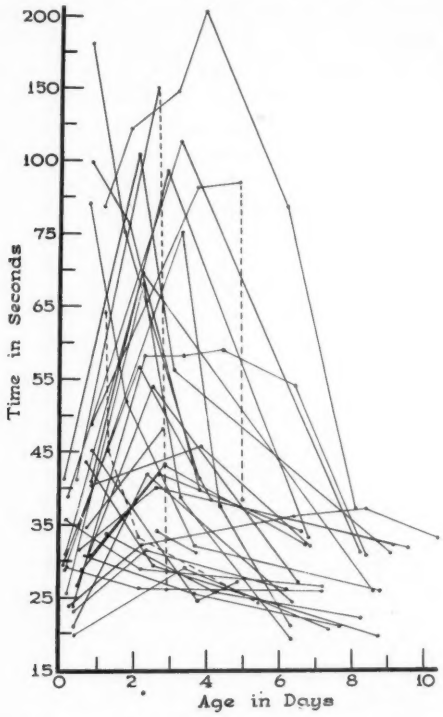

Fig. 1.—Microprothrombin times of 32 infants of untreated mothers. Broken lines represent the result of vitamin K therapy to the baby.

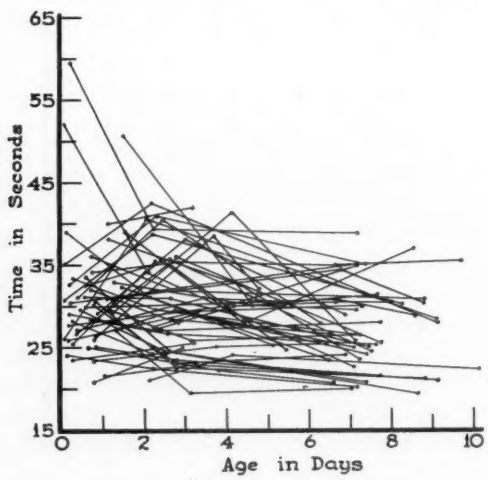

Fig. 2.—Microprothrombin times of 54 infants of mothers treated with vitamin K during labor.

monstrable difference between the two groups. Both fail to show the prolongation of prothrombin times ordinarily seen in the untreated cases.

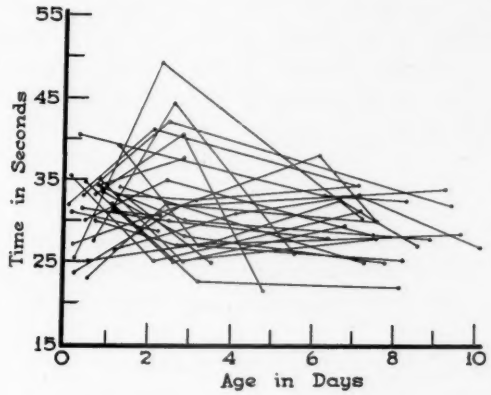

Fig. 3.—Microprothrombin times of 25 infants of mothers treated with vitamin K prior to labor.

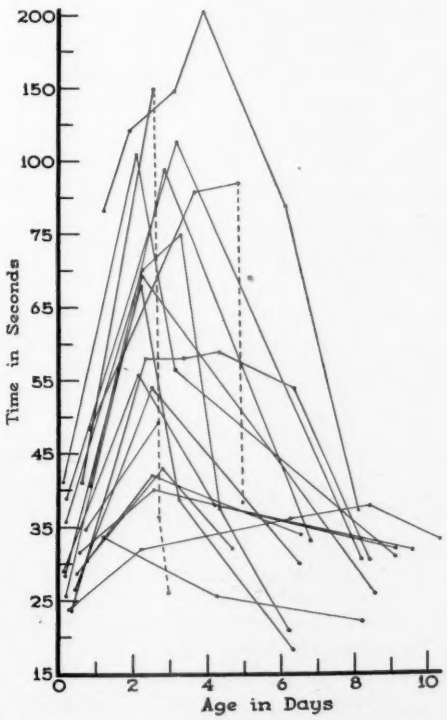

Fig. 4.—Microprothrombin times of 18 breast-fed infants of untreated mothers.

There was conspicuous difference between the breast-fed and the bottle-fed infants of untreated mothers with respect to the types of microprothrombin curves. Fig. 4 shows the breast-fed infants; in

general their microprothrombin times are much more prolonged on the second and third days than is true in the bottle-fed babies (Fig. 5). The latter tend to approach normal values rapidly without undergoing the prolongation characteristic of the breast-fed infants. Fig. 6 shows the contrast in prothrombin levels which occurred in double ovum twins after the first day; the breast-fed infant developed hemorrhagic disease which responded to menadione (case 1), while the bottle-fed baby maintained a normal course.

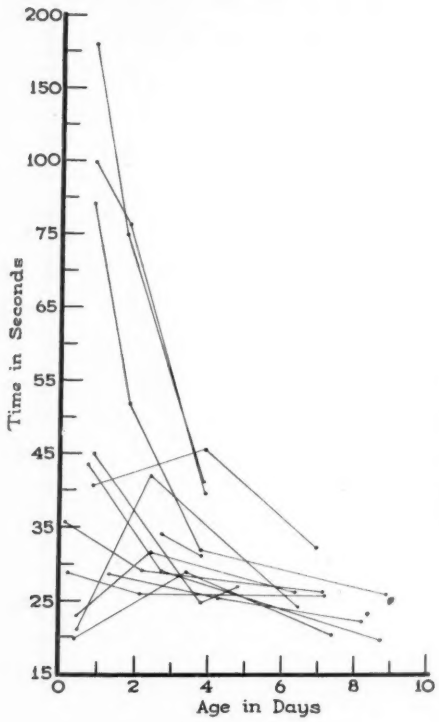

Fig. 5.

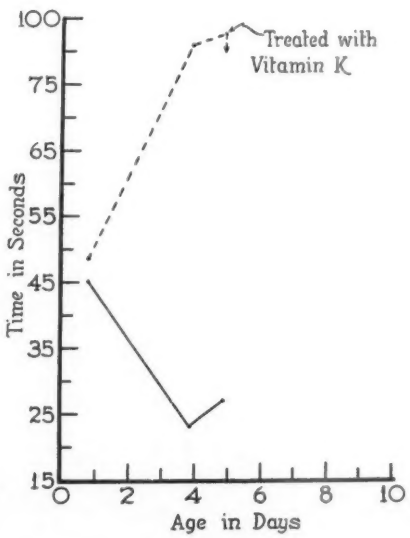

Fig. 6.

Fig. 5.—Microprothrombin times of 13 bottle-fed infants of untreated mothers.

Fig. 6.—Breast fed entirely _____, B. W., 3,470 Gm., male. Bottle fed entirely _____, B. W. 2,420 Gm., female. Microprothrombin times of binovular twins of an untreated mother. The larger infant was breast fed, the smaller bottle fed.

RETINAL HEMORRHAGES

Examination of the fundi was made in almost every infant; this was done during the first ten days, in the majority of cases during the first seventy-two hours. It is occasionally difficult to obtain a good view of the eye grounds during the first two or three days if the infant has chemical conjunctivitis. Ordinarily it may be done without too much difficulty if the pupils are dilated with homatropine, 0.5 per cent, and the baby appeased by means of a bottle containing sugar solution or formula.

Table I illustrates the striking decrease in the incidence of retinal hemorrhages in the infants of treated mothers as compared to the in-

TABLE I. INCIDENCE OF RETINAL HEMORRHAGES IN INFANTS OF MOTHERS (A) WHO RECEIVED NO VITAMIN K, (B) WHO RECEIVED VITAMIN K DURING LABOR, (C) WHO RECEIVED VITAMIN K PRIOR TO LABOR

TOTAL CASES	INCIDENCE OF HEMORRHAGES		SIZE OF HEMORRHAGES	
	NO. OF CASES	PER CENT	SMALL	LARGER
(A) 25 untreated cases	11	44	7	4
(B) 53 cases treated during labor	10	19	4	6
(C) 23 cases treated prior to labor	3	13	3	0

cidence among those who were untreated. There were retinal hemorrhages in 44 per cent of the untreated cases; some of the hemorrhages were fairly large; their incidence corresponds closely with that found in a previous study by McKeown[11] of 498 newborn infants. In the cases in which menadione was not given until after the onset of labor, retinal hemorrhages were present in 19 per cent; in over half of the cases the hemorrhages were moderately large. In the cases in which the mothers received menadione prior to labor, there were retinal hemorrhages in only 13 per cent; none of these hemorrhages were large. Statistical examination of these data by the method of chi-square demonstrates a highly significant difference between the infants of treated and those of untreated mothers; between the two treated groups there is no significant difference. However, the size as well as the number of hemorrhages provides some evidence that administration of menadione prior to the onset of labor may afford more effective prophylaxis. Maumenee and his associates[12] recently reported definite reduction in the incidence of retinal hemorrhages as a result of antenatal vitamin K therapy; this effect was significantly greater in the group treated before labor than in those treated during labor alone.

CASES OF HEMORRHAGIC DISEASE TREATED WITH VITAMIN K

CASE 1.—Y., colored male, one of double ovum twins, was born in January, 1941, following a labor of 15 hours and a spontaneous vertex delivery. Birth weight was 3,470 Gm. No vitamin K was administered to the mother; this was her second pregnancy. The infant was breast fed throughout the hospital stay, receiving, in addition, 5 per cent sucrose water during the first 3 days. Feedings were taken well; the weight dropped to a low figure of 3,120 Gm. on the fifth day; it was 3,270 Gm. on the tenth day. The microprothrombin time was 48.5 seconds on the first day, compared to a normal control of 25 seconds. Examination of the eye grounds on that day showed large and small flame-shaped hemorrhages above and below the optic discs. On the fourth day the microprothrombin time was 89 seconds, as compared with a control of 22 seconds. The next day the microprothrombin time was 93 seconds, with a control value of 18 seconds. The coagulation time was 4 minutes. It was discovered at that time that the heel prick from the previous day was still oozing, and vitamin K therapy was therefore thought to be indicated. Thyloquinone (2-methyl-1, 4-naphthoquinone) in oil, 2 mg., was given by mouth. One and one-half hours later the oozing had stopped; the microprothrombin time was 38 seconds, control 18 seconds. One and three-fourths hours after that the microprothrombin time was 43 seconds; the coagulation time was 2¼ minutes. An hour and one-half later the microprothrombin time was 37 seconds; the coagulation time had remained the same. The following morning, 23 hours after administration of vitamin K, the microprothrombin time was 19 seconds, with a control of 16 seconds;

the coagulation time was 1¾ minutes. Two days later the microprothrombin time was approximately the same. The baby was discharged on the tenth day in good condition.

The course of the other twin was in marked contrast to that of the boy just described (Fig. 6). The girl weighed 2,420 Gm. at birth; on formula feedings she gained satisfactorily and was 150 Gm. over birth weight by the tenth day. The microprothrombin time was normal after the first day.

CASE 2.—F., white male, was born during February, 1941, the second child of a normal mother, following a labor of 2 hours and a spontaneous vertex delivery. No vitamin K prophylaxis was given. Birth weight was 3,430 Gm. Moderate icterus appeared on the first day and persisted. Physical examination was otherwise negative and hemoglobin level and red and white blood cell counts were normal. The baby did well generally until the ninth day, when there was a small amount of oozing from the umbilical cord, which was beginning to loosen. On the tenth day profuse oozing from the umbilicus began suddenly, enough to soak through several abdominal binders and a number of gauze dressings before it was stopped. Microprothrombin time a few minutes after the onset of the bleeding had no end-point, and the coagulation time was longer than 15 minutes. Thyloquinone in oil, 2 mg., was given intramuscularly. Fifty minutes later there was still no end-point of the microprothrombin time, but the coagulation time was 5½ minutes; the bleeding had not diminished. A dressing moistened with epinephrine solution was applied with a tight binder, without demonstrable effect on the bleeding. More vitamin K (4 mg. of thyloquinone in oil) was given intramuscularly 25 minutes later, 1¼ hours after the first dose. Ten minutes later the coagulation time was 4¾ minutes, and bleeding time was 1¾ minutes. The red blood cell count and hemoglobin level were essentially as on the first day; there were 2 nucleated erythrocytes per 100 leucocytes. Microprothrombin time 2½ hours after the first injection of vitamin K was 106 seconds, with a control of 23 seconds. By that time the oozing had become slight, and had been so for about one-half hour previously. The microprothrombin time 4 hours and 5 minutes after treatment was begun was 58 seconds; coagulation time was 2½ minutes. Bleeding had practically stopped. Two hours and 50 minutes later the microprothrombin time was 35 seconds; coagulation time was 2 minutes. No bleeding whatever was occurring at that time. The following day, 22 hours after institution of therapy, the microprothrombin time was 29 seconds, control 24 seconds; coagulation time was 2 minutes. The values remained within normal limits after that time.

CASE 3.—M., white male, was born during December, 1940, the seventh child of a normal mother who received no medicinal vitamin K. Labor lasted 1½ hours; delivery was spontaneous. Birth weight was 3,930 Gm. The microprothrombin time on the first day was 41 seconds, control 16 seconds; the coagulation time was 3 minutes. The baby was breast fed throughout, and took feedings well; at the time of discharge on the ninth day he was 130 Gm. under birth weight. On the second day of life the eye grounds showed no retinal hemorrhages. The following day the microprothrombin time was 150 seconds, with a control value of 22 seconds; the coagulation time was 5½ minutes. Vitamin K (2-methyl-1, 4-naphthoquinone) in oil, 2 mg., was administered intramuscularly into the buttock. An hour and thirty-five minutes later the microprothrombin time was 52 seconds, and the coagulation time was 4 minutes. A heel prick made almost 3 hours before was still oozing. Two hours and five minutes after therapy the microprothrombin time was 36 seconds; the coagulation time was 2¾ minutes; oozing from the heel had stopped. Nine hours and twenty minutes after treatment the microprothrombin time was 26 seconds. The following day, a little less than 24 hours following the intramuscular vitamin K, the microprothrombin time was 27 seconds, with a control of 22 seconds. The course thereafter was uneventful.

DISCUSSION

Our results confirm the findings of others that the administration of vitamin K to expectant mothers either during the latter part of pregnancy or during labor results in approximately normal prothrombin

values in their infants and virtually eliminates the prolongation in prothrombin time which usually occurs in untreated cases between the second and fourth days of life. Menadione (2-methyl-1, 4-naphthoquinone) was used in treatment; it is one of the most potent preparations having vitamin K activity. This was given during the latter part of pregnancy in doses of 2 mg. three times a day in tablet form; it is likely that a dosage of 1 or 2 mg. daily would have accomplished the same result. Hellman and his associates[6] report better utilization of vitamin K in an oily medium than in pills made up with lactose. We did not try different amounts or different forms of the drug.

The dosage used during labor was 20 mg. in most cases; in a few instances in which 10 mg. were given, there was an equal prophylactic effect; again it is quite possible that smaller doses would have been equally effective. There was no direct correlation between the prothrombin times of the infant and the time interval between treatment and delivery except in one case in which less than an hour elapsed; in that case the microprothrombin times followed a curve typical of the untreated cases.

An incidental finding of some interest is that formula feedings during the first few days of life counteract the hypoprothrombinemia which occurs ordinarily in untreated cases if the baby is fed on the breast alone. In cases in which the initial prothrombin time was abnormally long, the introduction of formula feedings quickly brought the prothrombin time to a value close to normal. These findings agree with those of Salomonsen and Nygaard,[13] who attribute the difference to a more rapid development of intestinal flora in infants given supplemental feedings shortly after birth. They quote Almquist and his coworkers,[14] who found that some species of bacteria form a vitamin K active substance as a metabolic product. That this may not be the entire answer is suggested by a preliminary experiment in one of our infants who was given sulfanilylguanidine in full doses beginning twelve hours after birth; in spite of the fact that one might expect this drug to keep bacterial growth below usual levels in the intestinal tract,[15] the prothrombin time rapidly approached normal on formula feedings. It seems probable that the relative starvation during the first three days in breast-fed infants is the important factor in the failure to form prothrombin, but at present we are unable to go further than that. The vitamin K content of milk itself is said to be low.

The prompt curative action of menadione in oil in hemorrhagic disease of the newborn is shown in three such cases reported in detail. This acted with equal rapidity whether given by mouth or intramuscularly; the dosage was 2 mg. to 6 mg.; within two hours bleeding stopped entirely or almost completely in each instance. There was apparently no need to repeat the initial dose, although in one case associated with severe bleeding two injections were given about an hour apart. It is our feeling that the intramuscular route is the preferable one in severe cases, because the possibility of loss by vomiting is eliminated.

The microprothrombin time as measured in this study gives information which is accurate and easily obtained concerning the danger of

hemorrhagic diathesis of the newborn. The danger zone appears to be between 70 and 100 seconds, but the variability of the bleeding level is demonstrated by one case in which a microprothrombin time of more than 200 seconds was unaccompanied by pathologic bleeding. In the three cases of hemorrhagic disease the estimations of coagulation time were made by the capillary tube method. The correlation with the prothrombin times is fairly good. We have not obtained a coagulation time of more than 2½ minutes in the presence of a normal microprothrombin time.

The reduction in the incidence of retinal hemorrhages in infants of mothers receiving vitamin K is significant because of the possible relationship between retinal and intracranial bleeding. It is recognized that difficult labors and instrumental deliveries contribute to the incidence of intracranial hemorrhage;[1] McKeown[11] has shown that the same factors affect the incidence of retinal hemorrhage. The frequency of difficult labors in our series appears to be evenly distributed throughout the treated and untreated cases. Hellman and his coworkers[16] report a substantial reduction in intracranial hemorrhage and mortality rate in infants whose mothers were given vitamin K during labor. In our cases there were no symptoms of intracranial hemorrhage and no deaths. The extent of the protection afforded can be accurately evaluated only by observation of a larger number of cases. It would not be surprising if the incidence of hemorrhage were lower when vitamin K therapy is instituted prior to labor than when it is given during labor alone, because in some of the latter cases considerable pressure may be exerted on the infant's head before administration of vitamin K.

SUMMARY

A simple test requiring only a small amount of capillary blood was utilized in making multiple determinations of prothrombin values in newborn infants. The test as described is accurate enough for practical purposes.

Treatment of expectant mothers with menadione (2-methyl-1, 4-naphthoquinone) during the last days of pregnancy or during labor virtually eliminated the hypoprothrombinemia and tendency toward pathologic bleeding as a result of hemorrhagic disease which otherwise may occur during the neonatal period.

The incidence of retinal hemorrhages in the newborn was markedly reduced in infants of mothers treated with menadione during labor or prior to labor. Our results suggest that the reduction is greatest in the cases in which treatment is instituted before the onset of labor. These findings are of particular interest in their possible relationship to intracranial hemorrhage.

The introduction of formula feedings during the first few days of life counteracted hypoprothrombinemia. The mechanism of this action is still not known.

Three infants with hemorrhagic disease of the newborn were rapidly cured by administration of vitamin K. In two cases this was administered intramuscularly, and in one case by mouth.

REFERENCES

(1) *Salomonsen, L.:* Acta paediat. 27: Suppl. I, 1939. (2) *Brinkhous, K. M.:* Medicine **19:** 329, 1940. (3) Council on Pharmacy and Chemistry: J. A. M. A. **116:** 1054, 1941. (4) *Hellman, L. M., and Shettles, L. B.:* Bull. Johns Hopkins Hosp. **65:** 138, 1939. (5) *Shettles, L. B., Delfs, E., and Hellman, L. M.:* Ibid. **65:** 419, 1939. (6) *Hellman, L. M., Moore, W. T., and Shettles, L. B.:* Ibid. **66:** 379, 1940. (7) *Quick, A. J.:* Proc. Soc. Exper. Biol. & Med. **42:** 788, 1939. (8) *Ziffren, S. E., Owen, C. A., Hoffman, G. R., and Smith, H. P.:* Ibid. **40:** 595, 1939. (9) *Kato, K.:* Am. J. Clin. Path. **10:** 147, 1940. (10) *Lawson, R. B.:* J. Pediat. **18:** 224, 1941. (11) *McKeown, H. S.:* Tr. Am. Ophth. Soc. **38:** 510, 1940. (12) *Maumenee, A. E., Hellman, L. M., and Shettles, L. B.:* Bull. Johns Hopkins Hosp. **68:** 158, 1941. (13) *Salomonsen, L., and Nygaard, K. K.:* Acta paediat. **27:** 209, 1939. (14) *Almquist, H. J., Pentler, C. F., and Mecchi, E.:* Proc. Soc. Exper. Biol. & Med. **38:** 336, 1938. (15) *Marshall, E. K., Jr., Bratton, A. C., White, H. J., and Litchfield, J. T., Jr.:* Bull. Johns Hopkins Hosp. **67:** 163, 1940. (16) *Hellman, L. M., Shettles, L. B., and Eastman, N. J.:* AM. J. OBST. & GYNEC. **40:** 844, 1940.

THE USE OF ESTROGENS IN THE TREATMENT OF DYSURIA AND INCONTINENCE IN POSTMENOPAUSAL WOMEN

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THE study reported here stems from the observation that a number of women with disorders of micturition, consisting of urinary frequency, urgency, and incontinence, experienced relief of these symptoms while being treated with estrogens for the usual menopausal complaints. In order to determine the relationship of the estrogen therapy to the amelioration of the urinary symptoms, a group of postmenopausal patients with urgency, dysuria, and stress incontinence were selected for study and treatment.

METHODS AND MATERIALS

All patients were submitted to the routine gynecologic examination, urinalysis and observation cystoscopy. In order to determine, objectively, whether these women were suffering from estrogen deficiency, and also to evaluate the efficacy of the administered hormone, vaginal smear studies were performed during the period of preliminary observation and after the institution of estrogen therapy. The aqueous fuchsin technique for staining the vaginal smears[1, 2] was employed. (In 3 patients, the vaginal smear studies were supplemented with vaginal biopsies.)

A series of 16 cases was investigated. Six patients complained of urinary frequency, burning sensation on urination, and urgency; 10 complained also of incontinence on coughing, sneezing, or straining. The ages ranged from 57 to 72 years. Of the 16 patients, 10 were multiparas (para ii to xii); 2, primiparas; 1, nullipara; and 3, virgins. Four of the patients had moderate cystoceles and 2 urethroceles; 6 had clinical evidence of senile vaginitis. In the others, except for the presence of genital atrophy, consistent with the ages of the patients, there was no palpable pelvic organic disease. Cystoscopic examination revealed, in the majority, slight congestion of the trigone; in 2 there was also slight edema of the bladder sphincter. Repeated urinalysis in all of these patients failed to reveal a cause for the symptoms. The preliminary vaginal smears in all revealed cytologic evidence of marked estrogen deficiency.

THERAPY

As soon as the preliminary investigations had been completed, the patients were placed on estrogen therapy. The estrogens used were estradiol benzoate* (4,000 to 10,000 R.U., 2 or 3 times weekly) and estradiol dipropionate† (1 or 2 mg., 3 times weekly, or 5 mg., once or twice weekly) in solution in sesame oil, administered intramuscularly.

RESULTS

Some symptomatic improvement was noted in 7 cases as early as one week after the beginning of treatment, coincident with the appearance of estrogenic effect in the vaginal mucosa (Figs. 1, 2, 3, 4, and 5). At the end of two weeks, there was definite relief of symptoms in 12 of the 16 cases. With the exception of 3 cases (one of which was only moderately improved and 2, unimproved), the symptoms were completely controlled at the end of the fourth week of treatment.

Following the discontinuation of treatment, the patients remained symptom free for periods varying from six weeks to four months. Thereafter, symptoms returned with progressive severity. It was noted that recurrence of symptoms was accompanied by evidence of estrogen deficiency in the vaginal smears. These patients were subsequently given additional courses of estrogen therapy which resulted in disappearance of the symptoms. In several patients, the same cycle (recurrence of symptoms upon withdrawal of estrogens, followed by relief of symptoms after reinstitution of estrogen therapy) was repeated several times during the course of three years. The case history of one patient who has been under observation by one of us (U. J. S.) for 5 years, during which time she experienced 4 recurrences of symptoms, each time associated with characteristic estrogen deficiency smears, is given in detail. At each recurrence, symptoms responded promptly to estrogen therapy.

Case G. D., aged 56 years, was a gravida v, para iii, youngest child aged 27. Menstrual history, 14 by 28 by 5; menopause occurred at 51 years of age. The patient was first seen on Oct. 12, 1935, complaining of urinary incontinence which began shortly after the menopause and had grown steadily worse during the following two years. In addition, she complained of urinary frequency, dysuria, and vaginal irritation. General physical examination revealed nothing relevant. Pelvic examination revealed the orifice of the urethra to be markedly reddened and the surrounding mucosa to be spotted with minute, reddish erosions. The vaginal mucosa exhibited a characteristic picture of senile vaginitis. On straining, a small cystocele and urethrocele were evident. The uterus was atrophic, pelvic examination being otherwise negative. The vaginal smear and biopsy revealed an advanced degree of estrogen deficiency (Figs. 1 and 2). Cystoscopic and urinary examination were essentially negative. A diagnosis of senile vaginitis, urethrocele, and cystocele was made. The urinary incontinence was attributed to the urethrocele and cystocele. It was planned to do a urethroplasty for the cure of the incontinence; but, because of the senile vaginitis, it was felt advisable to treat this condition prior to operation. Accordingly, the patient was given 4,000 R.U. of estradiol benzoate, intramuscularly, 3 times weekly. At the end of one week, after a total of 12,000 R.U., the patient reported slight improvement and the vaginal smear revealed a definite, though incomplete, estrogen effect (Fig. 3).

*For the estradiol benzoate (progynon-B) and the estradiol suppositories used in this investigation, we are indebted to Drs. Erwin Schwenk and Max Gilbert, of the Schering Corporation, Bloomfield, N. J.

†For the estradiol dipropionate (di-ovocylin) used in this investigation, we are indebted to Mr. Robert C. Mautner, of Ciba Pharmaceutical Products, Summit, N. J.

Two weeks later, after a total of 36,000 R.U., the urinary symptoms, including the incontinence, were completely relieved. With a full bladder, and in the lithotomy position, the patient was not incontinent on coughing or straining. The eroded areas surrounding the urinary meatus were completely epithelized, the

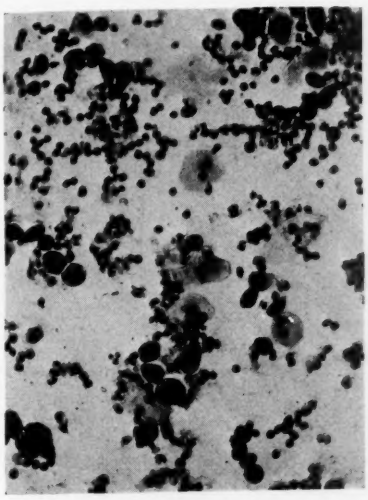

Fig. 1.

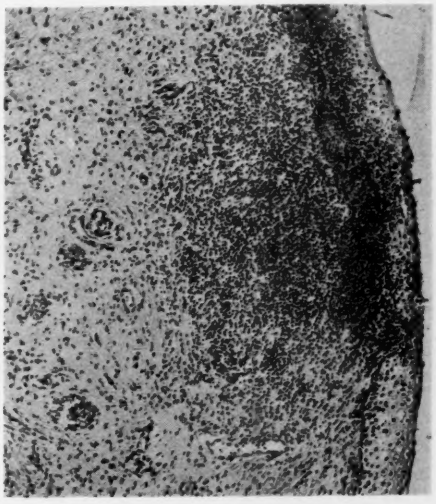

Fig. 2.

Fig. 1.—Case G. D., aged 56 years, gravida v, para iii, had a natural menopause, 5 years previously. Complaints: dysuria and incontinence. Pretreatment vaginal smear (Oct. 12, 1935) revealed "atrophy" cells, leucocytes, and erythrocytes, characteristic of advanced degree of estrogen deficiency and senile vaginitis. (×200.)

Fig. 2.—Pre-treatment vaginal biopsy taken at same time as smear in Fig. 1. Note atrophied epithelial layer, absence of cornification, intraepithelial and subepithelial leucocytic infiltration, characteristic of advanced degree of estrogen deficiency and senile vaginitis. (×100.)

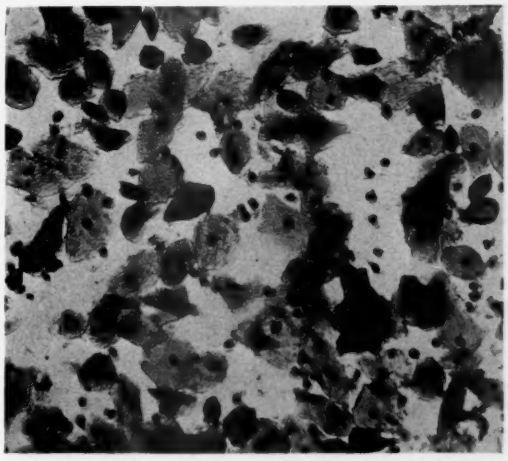

Fig. 3.—Case G. D. Vaginal smear (taken one week later) following the administration of 12,000 R.U. of estradiol benzoate. Slight symptomatic improvement. Note decreased number of leucocytes and "atrophy" cells; advent of large, squamous epithelial cells, indicating estrogenic effect (incomplete). (×200.)

vaginitis had completely disappeared, and the vaginal mucosa had a healthy, pinkish color. The vaginal smear and biopsy, at this time, revealed a full estrogenic effect (Figs. 4 and 5). The patient was then given 4,000 R.U., every two

weeks, for the following six weeks. She remained symptom-free for six weeks thereafter, without further treatment.

On April 22, 1936, the patient reported that the dysuria, urinary frequency, and incontinence had recurred several weeks before. Examination revealed a slight erosion of the urethral meatus and a moderate degree of senile vaginitis. The vaginal smear revealed a slight degree of estrogen deficiency. The patient

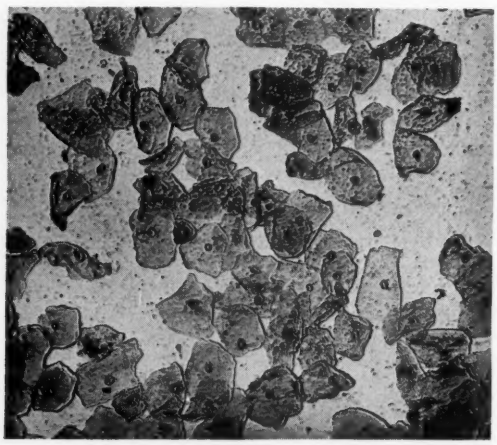

Fig. 4.—Case G. D. Vaginal smear taken three weeks after beginning of treatment, following total of 36,000 R.U. of estradiol benzoate. Incontinence and dysuria completely relieved. Note absence of leucocytes and "atrophy" cells and their replacement by large, squamous epithelial cells with small nuclei, indicating full estrogenic effect. (×200.)

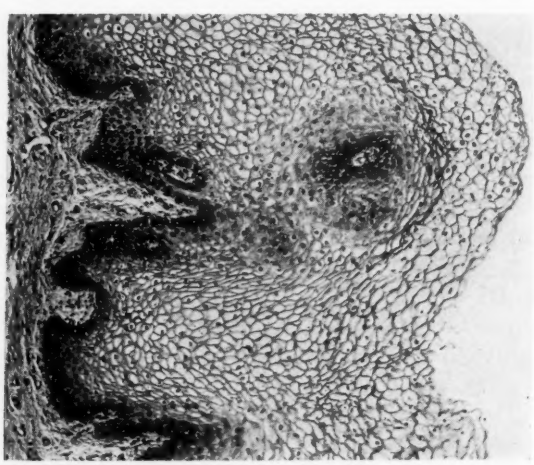

Fig. 5.—Posttreatment vaginal biopsy taken at same time as smear in Fig. 4. Compare with Fig. 2. Note increased thickness of epithelial layer; vacuolization, marked proliferation of basalis, absence of leucocytic infiltration. This histologic picture is indicative of a full estrogenic effect and is comparable to the vaginal mucosa in cyclical women with normally functioning ovaries. (×100.)

was then given 10,000 R.U. of estradiol benzoate and the same dose was repeated twice weekly. At the end of two weeks the symptoms were again completely relieved and the vaginal smear showed complete estrogenic effect. At this point, the patient developed uterine bleeding which continued for five days. She was, thereafter, given 10,000 R.U., every two weeks, for the following four months. The patient then remained symptom-free for four months without additional therapy, after which symptoms again recurred. Examination of the vaginal

smear again revealed evidence of estrogen deficiency. During the following three years, the patient experienced 2 additional recurrences associated with vaginal smear evidence of estrogen deficiency. In each instance, treatment with estrogens resulted in prompt relief of the symptoms, paralleled by estrogenic changes in the vaginal smears.

In order to prevent recurrence of symptoms, it became our practice to place these patients on maintenance doses of estrogens. This was accomplished with intramuscular injections of estradiol benzoate or estradiol dipropionate, every two to four weeks, or with estradiol vaginal suppositories (2,500 R.U.), 2 or 3 times weekly. The dose of estrogens necessary to keep the patient adequately supplied varied in different patients and required individual adjustment. Vaginal smear examinations at intervals of two to four weeks were performed to insure the adequacy of the estrogen dose.

COMMENT

The orthodox treatment of functional disorders of micturition, with or without stress incontinence, in elderly women, which consists of bladder irrigations, silver nitrate instillations, etc., is frequently attended by poor or indifferent results. In 10 of the cases reported here, the urinary symptoms could not be accounted for on the basis of any demonstrable disease in the urinary tract. Six patients, however, had clinical evidence of obstetric trauma, viz., moderate cystoceles or urethroceles. The possibility of an anatomic lesion in the sphincter mechanism playing a role in the etiology of the urinary symptoms in this group cannot be excluded. However, it is noteworthy that the symptoms in these cases did not appear until after the menopause. This leads us to believe that if the anatomic lesions were involved at all in the genesis of these symptoms, they acted only in an accessory role. Furthermore, this study revealed the fact that 4 of the patients with incontinence were never exposed to the trauma of labor, 3 of them being virgins. This observation eliminates the possibility of ascribing the incontinence, in these cases, to an anatomic defect of the bladder sphincter resulting from parturition. It is evident, therefore, that urinary frequency, urgency, dysuria, and incontinence can occur in elderly women without evidence of organic disease or of anatomic defects in the urinary tract, and without exposure to the trauma of parturition.

This study disclosed one factor common to all of these cases, viz., morphologic evidence of estrogen deficiency. The striking results obtained with estrogen therapy, in the majority of these cases, and the recurrence of symptoms associated with re-appearance of signs of estrogen deficiency following estrogen deprivation, lead us to believe that estrogens play a role in the physiologic processes involved in normal micturition in women.

The question arises as to the modus operandi of the estrogens. The muscle fibers of the bladder sphincter are intimately related anatomically (and probably also embryologically*) to the muscularis of the

*The bladder appears to be formed partly from the ends of the Wolffian ducts and partly from the entodermal cloaca. According to Berry Hart, the lower third of the vagina is formed by the coalescence of the upper portion of the urogenital sinus and the lower ends of the Wolffian ducts, and the epithelial lining of the vagina is derived from the Wolffian bulbs.[6] It is tempting to believe that the bladder sphincter, which shares a common embryologic component with the vagina, may be under the influence of the same hormonic stimulus as the latter, viz., the estrogens.

vagina. Furthermore, both the histologic and physiologic integrity of the vagina are dependent upon an adequate supply of estrogens. Prolonged estrogen deprivation leads to a marked decrease in blood supply to the vagina and to atrophy of the muscularis as well as of the mucosa of the vagina. It seems logical to expect that these striking involutional changes would also affect the bladder sphincter, either directly, by impairing the intrinsic tone of its muscle fibers, or indirectly, because of the atrophy and atony of the muscularis of the vagina.

The relationship of the dysuria and urinary frequency to the estrogen deficiency still remains to be explained. The "trigonitis" which one finds so frequently in these patients, we believe, is an incidental finding, since similar degrees of congestion of the trigone are found without symptoms. We have been impressed with the fact that all of the patients with these symptoms had, in addition to advanced degrees of vaginal atrophy or senile vaginitis, a similar atrophic process involving the orifice of the urethra and the surrounding mucous membrane. The mucosa in these regions exhibited pin-point hemorrhagic and eroded areas. Urine coming in contact with the eroded areas causes pain, burning, and urinary frequency. Following treatment with estrogens, the pin-point erosions disappear and the meatus and periurethral mucosa, like the vaginal mucosa, become completely epithelized, assuming a smooth, uniformly pink appearance, coincident with relief of symptoms.

The 3 patients who did not respond satisfactorily to the estrogen treatment have remained unsolved problems. In 2 of these, the presence of an anatomic defect (cystocele) may account for the persistence of the symptoms, although other patients with lesions of apparently similar degree were benefited very strikingly by estrogens. Surgical repair was not feasible in these cases because of cardiovascular disease. The third patient was a virgin. Apparently incontinence may be attributable to still other factors aside from anatomic defects in the sphincter mechanism or estrogen deficiency. The possibility of psychogenic factors has been considered, and these patients are being studied from this angle.

The question arises as to why do not all elderly women develop urinary symptoms. The same question may be raised with regard to senile vaginitis. The answer appears to lie in the fact that not all postclimacteric women suffer from an estrogen deficiency. There is evidence which indicates that some women apparently produce estrogens for many years after the menopause or even after bilateral ovariectomy. Thus, some women exhibit morphologic evidence in the vaginal mucosa of estrogenic stimulation many years after the menopause[1, 2] and excrete estrogens even after bilateral ovariectomy.[3, 4] It is conceivable that the endogenous estrogens, which experimental evidence indicates are probably formed in the adrenal cortex,[5] may prevent the estrogen deficiency and its concomitant symptoms, for many years after the menopause.

On the basis of the observations reported here, we would suggest that elderly women with urinary incontinence be examined for estrogen deficiency before resorting to surgical measures, and, if signs of

an estrogen deficiency are found, such patients, regardless of the presence of an organic lesion (e.g., cystocele or urethrocele), should be given a therapeutic test with estrogens.

SUMMARY AND CONCLUSIONS

1. Sixteen postmenopausal women with urinary symptoms (urinary frequency, urgency, and incontinence), which were refractory to orthodox treatment, were found to have an estrogen deficiency.

2. Acting on the assumption that the urinary symptoms were related to the estrogen deficiency, these patients were treated with estrogens.

3. Relief of symptoms was achieved in all but 3 cases.

4. Relief of symptoms ran parallel with evidence of estrogenic effect in the vaginal smears.

5. Symptoms recurred gradually after the discontinuation of therapy, coincident with the re-appearance of signs of estrogen deficiency in the smears.

6. Patients could be kept symptom-free on a maintenance dose of estrogens.

7. On the basis of the observations reported here, it is concluded that: (a) a syndrome consisting of urinary frequency, dysuria, and incontinence in elderly women can be caused by a long-standing estrogen deficiency; (b) in advanced stages, the estrogen deficiency leads to atrophic erosions of the mucous membrane of the urethral meatus similar in appearance to the erosions in "senile vaginitis"; this "senile urethritis and periurethritis" causes urgency, painful micturition, and frequency; (c) the estrogen deficiency also leads to impairment of the bladder sphincter function which results in incontinence.

8. It is suggested, on the basis of these observations, that postmenopausal women, upon whom vagino- or urethroplasty is contemplated for the relief of incontinence, whether or not a cystocele or urethrocele is present, be examined for evidence of estrogen deficiency, and, if such a deficiency is found, that they be given a full course of estrogens as a therapeutic trial.

REFERENCES

(1) *Salmon, U. J., and Frank, R. T.:* Proc. Soc. Exper. Biol. & Med. **33**: 612, 1936. (2) *Geist, S. H., and Salmon, U. J.:* Am. J. Obst. & Gynec. **38**: 392, 1939. (3) *Frank, R. T., Goldberger, M. A., and Salmon, U. J.:* Proc. Soc. Exper. Biol. & Med. **33**: 615, 1939. (4) *Fluhman, C. F., and Murphy, K. M.:* Am. J. Obst. & Gynec. **38**: 778, 1939. (5) *Salmon, U. J.:* Proc. Soc. Exper. Biol. & Med. **41**: 515, 1939. (6) *Hart, B.:* Gray's Anatomy, ed. 21, 1216, Philadelphia, 1924, Lea & Febiger.

Machado, Lucas M.: Tuberculosis of the Breast, Rev. de gynec. e. d'obst. **34**: 326, 1940.

The author reviews the literature and presents a lengthy anatomic and pathologic discussion of the etiology of tuberculosis of the breast. It is suggested that radical mastectomy be performed for the primary type, the prognosis of which is good. In the secondary types, the treatment is general and palliative; the prognosis in this latter group is poor.

Mario A. Castallo

ROLE OF CARBON DIOXIDE IN RESUSCITATION AT BIRTH AFTER ASPHYXIA AND AFTER NEMBUTAL ANESTHESIA*

An Experimental Study in the Cat and Guinea Pig

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THE observations to be reported are part of a broader study of the physiology of respiration in the fetus and newborn. No attempt will be made to correlate the dosages of nembutal we have used with those commonly or uncommonly employed in the human being. From the standpoint of experimentation it is permissible and often desirable to study exaggerated effects; this we have done with no thought as to whether or not you might have occasion to employ comparable amounts of the drugs.

In February of last year Dr. Yandell Henderson addressed a letter to the Editor of the *Journal of the American Medical Association,* in which he proposed a new word in anesthesia. He suggested *anarchapnea,* containing the Greek roots "archon" (governor) and "pneuma" (breath), to indicate a state of uncontrolled respiration encountered after excessive use of certain narcotic drugs, notably the barbiturates. The government of respiration by carbon dioxide appears to be abolished in deep barbiturate narcosis. The responsiveness of the respiratory center is lowered, the volume of breathing diminishes, hypercapnia manifesting itself as carbon dioxide displaces oxygen in lung alveoli, and anoxia ensues.

The use of carbon dioxide diluted in oxygen for resuscitation in asphyxia of the newborn has been debated for some years. One group of obstetricians report that they have used carbon dioxide advantageously, while another group holds that it is definitely contraindicated. Henderson suggested that both may be correct. Those who favor its use have employed no barbiturates or have used them sparingly. Those who have had adverse experiences with carbon dioxide have induced narcosis, often deeply, with the barbiturates, and the babies may well have been in a state of anarchapnea in which carbon dioxide could not stimulate breathing.

We were particularly interested in Henderson's suggestions, because we had had some similar experiences in resuscitating newborn kittens, asphyxiated in the course of studying respiration during birth. Since then we have taken care to observe the effects of carbon dioxide in oxygen-air mixtures used to resuscitate after asphyxia and after barbiturate narcosis.

We have studied intrauterine respiratory activities in several hundred fetuses of several species during the last few years. Respiration at birth

*Read at a meeting of the Chicago Gynecological Society, May 16, 1941.

under normal and asphyxial conditions has engaged our attention in at least 50 litters of kittens and guinea pigs. The effects on the fetus of nembutal administered to the mother have been observed in 25 pregnant cats with 88 fetuses, for the most part within five days of birth, and about a dozen guinea pigs at full term.

A variety of experimental procedures have been used. The pregnant guinea pig lends itself well to operations after local anesthesia of the abdomen. This method cannot be used in cats successfully. It has been our practice to decerebrate most of these animals by ligating carotid and basilar arteries by the Pollock and Davis technique under ether an hour or more before starting to deliver their fetuses. This makes it possible to perform experiments on the fetuses without using anesthesia of any type.

Elsewhere we have described the physiology of respiration in utero at some length, but because it forms the basis for understanding our present subject we shall review it very briefly.

In the first place, a number of factors combine to insure an adequate supply of oxygen to the fetus. The blood reaching the fetal brain is rather well saturated with this gas throughout most of prenatal life. Upper limits of 90 per cent or more have been observed in experiments in sheep. Toward the end of gestation a physiologic partial anoxemia manifests itself as the efficiency of the placenta declines and fetal metabolic needs increase; the oxygen content of the blood going to the fetus decreases. It is erroneous, however, to conclude that a true anoxia is ever present, even at full term. In the cat, the partial anoxemia encountered at the end of gestation is relieved phasically by action of the uterine musculature.

In the latter part of gestation the cat fetus exhibits certain activities periodically as the uterine tonus waxes and wanes. With each uterine contraction the oxygen content of the blood passing from placenta to fetus rises, the fetal heart rate increases, fetal motor activities decrease and intrauterine respiratory movements are not observed. During the relaxed state of the uterus the oxygen content of the umbilical vein blood falls, the fetal heart rate declines, the fetus becomes active again, and occasionally brief, rapid rhythms of shallow, intrauterine respiratory movements occur. It is evident that these phenomena are associated with an anoxemia which is relieved by the contraction of the uterus, at least under conditions of experimentation with the animal's abdomen incised. To what extent they occur in the normal intact individual we do not know, but on only one occasion have we seen intrauterine fetal respiratory movements in an unanesthetized or unoperated cat and never in guinea pigs. Atmospheres low in oxygen or containing an excess of carbon dioxide when breathed by the mother do induce intrauterine respiratory movements in the apneic fetuses.

When a fetus is born normally or is delivered without anesthesia, the stimulus of the anoxia associated with interruption of placental exchange serves as an exaggeration of the stimulus of the intrauterine anoxemia associated with uterine relaxation; the fetal heart slows, the fetus squirms, and breathing starts at once. The blood becomes well oxygenated again due to pulmonary breathing, but the newborn does not

lapse into apnea as it did in utero. It seems that the changed environment with markedly increased afferent stimulation lowers the threshold of the respiratory center.

When a cesarean section is performed in a decerebrated cat without general anesthesia and the uterine vessels are clamped to bring about anoxia in the fetus, the fetal heart beat slows to half or less than half its normal rate, motor activities are exaggerated and deep respiratory movements are initiated. These cause aspiration of the amniotic contents. Such an asphyxia can be prolonged in the cat for fifteen or twenty minutes and in the guinea pig for five to seven minutes. Respiratory movements become deep gasps at ten- to forty-second intervals. It has been our experience that the fetus must be delivered before these cease, to ensure spontaneous respiration. When this is done, breathing is established by the gasps, and normal respiratory movements are later superimposed upon the gasp rhythm as oxygenation of the blood takes place. Although no special measures were usually necessary, oxygen-air mixtures appear to speed resuscitation. When small quantities of carbon dioxide were added, the depth and sometimes the rate of the respirations were observed to increase. Recovery from simple asphyxia was usually complete within an hour or two in the cat, but symptoms of central nervous system damage, persisting for several days (even weeks in one case), were observed in a few animals, especially in the guinea pigs.

A very different picture of respiration at birth presented itself when nembutal was given to the mothers. The usual procedure was as follows: cesarean section was performed without anesthesia or under local anesthesia, and one fetus was delivered for control. It breathed at once. Nembutal was then administered intravenously to the mother. An anesthetic dose for adult animals was considered to be 28 mg. per kilo of body weight. In a few experiments, this amount was given. In some experiments as little as one-fourth of an anesthetic dose was used. Five minutes time was allowed between administering the drug and delivering the second and third fetuses. Following this, additional amounts of the drug were given (usually 7 mg. per kilo) and the remaining fetuses were delivered after another five minutes. In no experiment was more than a total of 28 mg. per kilo given.

After a full anesthetic dose of nembutal had been administered to the pregnant cats, the fetuses were profoundly narcotized. Some could not be induced to breathe. Others gasped feebly at rates of less than four times per minute. Most of them died within two hours. They were completely flaccid and appeared to draw little air into their lungs.

When approximately 20 mg. of the drug per kilo had been used, the fetuses were completely narcotized. They did not often begin to breathe for several minutes after delivery. Respirations then were gasps beginning slowly, and gradually increasing from two to about 10 or 15 per minute in the course of several hours. These gasps were less deep than those observed in nonnarcotized animals born after uncomplicated anoxia. They appeared to be less effective in drawing air into the lungs because hypotonus of the musculature did not allow adequate chest ex-

pansion. Although some air did enter the lungs of most of them, normal rhythmical breathing did not usually occur until the narcosis had begun to subside. Some of these fetuses died in a cyanotic condition. They appeared to be asphyxiated in spite of their efforts to obtain air.

When one-fourth to one-half of an adult anesthetic dose of nembutal had been administered, the fetuses nearly always began to breathe within one or two minutes. Here too, respirations were slower than normal, often even slower than those of fetuses delivered after prolonged anoxia. The volume of breathing appeared to be lessened in the newborn under these dosages of nembutal. Initial respirations were not so deep as those encountered in the normal control animals.

The effects of nembutal upon the newborn cat and guinea pig fetuses lasted from several hours to two days, depending on the depth of the narcosis. Even when less than 14 mg. per kilo had been given to the mothers, the young animals did not begin to move about for an hour or more. Often they failed to nurse for the first day and probably obtained little nourishment for several days because of the residual lethargy.

As soon as possible after delivery and when it had become evident that the narcotized newborn animals had established regular, though often very slow rhythms of breathing, they were placed in warm chambers of 70 liters capacity. In one chamber, oxygen was added to the air; in another a mixture of oxygen (90 per cent) and carbon dioxide (10 per cent) was added. In a few experiments the carbon dioxide content was raised further by adding a small quantity of the undiluted gas to the latter mixture.

The mixtures of carbon dioxide in oxygen had no visible beneficial effect on the respiration of any narcotized cat fetus for the first hour or two after birth. A few of the guinea pigs, not so heavily narcotized and already executing more normal rhythms of breathing, did respond to the carbon dioxide. Heavily narcotized cat fetuses died when left in the carbon dioxide mixtures for several hours, although several recovered in atmospheres containing a high percentage of oxygen alone. Cyanosis was relieved and regularity of breathing improved as recovery from the narcosis gradually took place.

The newborn animals delivered after doses of about one-half anesthetic value were especially interesting. Litter mates were delivered simultaneously and placed in the warm chambers, one in oxygen-air mixture and the other in oxygen-carbon dioxide-air mixture. No difference in the rate or depth of their respirations could be observed for more than two hours. It was perfectly clear that their breathing was unaffected by the powerful respiratory stimulant, carbon dioxide. As soon as the narcosis began to subside and the animals began to move about, we could observe an increase in depth of respirations of the specimens in the carbon dioxide mixture. Later this was occasionally followed by an increase in the rate as well. The respirations of the animals in the oxygen-air mixtures increased in rate but decreased in depth at the time the narcosis subsided. Ultimately they became equal to those of the nonnarcotized control animals.

In attempting to interpret our results, the concept of Yandell Henderson is especially valuable. It would seem that excessive but subanesthetic doses of nembutal administered to pregnant cats and guinea pigs engendered states of anarchapnea in the fetuses. Delivery during the anarchapnea brought forth newborns which quickly became hypercapnic (i.e., their blood carbon dioxide level increased), and gasped only under the stimulus of anoxia. Administration of carbon dioxide only added to the hypercapnia and did not alter the respiratory response. In profound anarchapnea, air alone was insufficient for resuscitation, probably because the high content of carbon dioxide in the newborn lungs excluded oxygen (as the tension of one gas goes up the other must go down). During anarchapnea, oxygen administration was necessary to prevent asphyxia while the newborn was recovering from the narcosis.

The authors wish to acknowledge financial aid from The Women's Faculty Club of Northwestern University Medical School.

DISCUSSION

DR. FRANKLIN F. SNYDER.—Dr. Windle has pointed out the dosage level at which deep depression and disorganization of respiratory regulation occur following intravenous administration of pentobarbital. In cats, it is stated that less than 30 mg. per kg. may result in depression of respiration to a level as low as 2 per minute. Normal oxygenation of the blood would be reduced in addition to the depression of the central nervous system.

At this level of activity of the respiratory system one is studying the abnormal and must be prepared for apparently paradoxical findings. This has turned out to be the case with regard to the administration of CO_2 and oxygen. Marshall and Rosenfeld, in 1936, demonstrated that in cats deeply depressed by pentobarbital and anoxemic, the administration of 5 per cent CO_2 in oxygen, instead of stimulating respiration, caused further depression or even apnea and death from respiratory failure. Under controlled conditions it was shown that oxygen, however, and not Co_2 was responsible for this effect. It depended upon the fact that in animals, deeply depressed, respiration may be maintained almost entirely by an anoxemic stimulus, so that oxygen by removing this stimulus depresses or abolishes respiration.

Experiments on denervation and freezing of the sino-aortic mechanism indicated that administration of oxygen was equivalent to a removal of stimuli acting mainly, if not entirely, through this mechanism. When severe depression by oxygen was observed, the addition of CO_2 to the oxygen failed to prevent this depression.

I cite these experiments to illustrate that different responses are elicited at different levels of respiratory activity corresponding to the degree of injury of the respiratory system. At the present stage of Dr. Windle's experiments, it seems to me that the role of CO_2 in the final results still remains to be defined.

Dr. Windle mentioned also a state of uncontrolled breathing in the newborn as a result of narcosis. Another example of this interesting condition comes to mind. In normal rabbit fetuses delivered prematurely, Rosenfeld and I obtained kymograph tracings of respiratory activity at an early stage of development before regulation by CO_2 and low oxygen was demonstrable.

DR. C. E. GALLOWAY.—In order to transfer these studies to practical use we could probably come to this conclusion: If we are dealing with a narcotized baby when we have used nembutal, it apparently will pay us to use oxygen instead of a mixture of oxygen and carbon dioxide.

Another point I gathered especially from Dr. Snyder's remarks is that when you are dealing with a premature baby, you should be careful about any anesthetic drug. Probably a local anesthesia would be better than a drug like nembutal that

causes depression of the respiratory center. In such a case we are apparently dealing with an individual who does not respond to respiratory stimuli in the same way that a full term baby does.

I am wondering what would happen to a baby if you gave the mother doses of nembutal equivalent in amount to those used on animals in these experiments five minutes before the baby was born. Twenty-eight to 30 mg. of nembutal per kilo of body weight means ½ gr. per kilo. My patients average 146 pounds at the time they deliver. That means if we give a woman 30 mg. per kilo we would give her about 36 gr. of nembutal. I am afraid this would kill the baby.

I would like to ask these men why they do not do experimental work with amounts of anesthesia in the animal comparable to those we used in practice. For instance, we get along very nicely with 6 gr. of nembutal in the average case. That amount constitutes about one-fifth to one-sixth of the dose used in these experiments.

There is one great fault with the barbiturates and that is the small margin between the anesthetic and the lethal dose. With intravenous anesthesia with barbiturates you had better have some method of artificial respiration ready. It is a dangerous anesthetic at the present time, and I think we should be very careful in using it, especially intravenously.

DR. WINDLE (Closing).—I think we have adequate controls in our present experiments because of the fact that in each experiment we delivered one fetus without anesthesia and without narcosis, and this served as control. The rest of them then were delivered under nembutal anesthesia or after asphyxia had been set up by clamping the umbilical or uterine vessels.

I am not quite sure how far we agree at present on the subject of intrauterine respiratory movements. We do agree on the fact that intrauterine respiratory movements can be obtained under certain conditions. Carbon dioxide certainly induces them in the apneic fetuses of the cat. I would like to ask how many obstetricians have actually seen these movements in the human being under normal circumstances. I have yet to find one who has seen them frequently. In fact, most men tell me that they have never seen them at all.

Dr. Galloway's practical interpretation is essentially correct. As I said in my preliminary remarks, we have no axe to grind in respect to the use of barbiturates in obstetrics. I do not know what would happen if you gave a mother 36 gr. of nembutal intravenously five minutes before the baby was born, but I expect that you would have a much depressed baby. We never used more than ½ gr. per kilo in any pregnant cat; usually half of this or less. The smallest total dosage was about equivalent to 7 gr. in a human being weighing 146 pounds. It is certainly true in the cat that when we gave a full anesthetic dose, we had great difficulty getting the newborn to survive. We have never lost a mother cat under those circumstances. The lethal dosage may vary for different animals and is about twice our anesthetic dosage for cats. Guinea pigs do not seem to be as much affected as cats.

The total blood volume of the human newborn has been found to be about 365 c.c. The oxygen capacity of the blood is approximately 21.5 volumes per cent. Utilization of oxygen (at least in the sheep fetus) is at the rate of 4.3 c.c. per kilogram per minute. If the blood of the newborn is 50 per cent saturated, there is a reservoir of about 40 c.c. of oxygen in the blood stream of the newborn. Thus a 3 kilogram baby would have a four-minute supply of oxygen. You know that babies do not die in four minutes of apnea.

That brings up another point, one that has been emphasized recently by Himwich. This investigator has shown that the survival time of the newborn rat is very long (fifty minutes) in comparison with the adult survival time (two to three minutes), but when he injected iodoacetate into the young rat, its survival time decreased to the adult survival time. Thus he gave us evidence that survival time is facilitated by anaerobic glycolysis in the newborn and does not depend entirely upon the amount of oxygen in the blood stream.

In regard to the question about the use of the tracheal catheter, I might say that we have performed a series of interesting experiments in guinea pig fetuses. After asphyxiating them until the respiratory movements stop in utero, we have not had one fetus start to breathe spontaneously thereafter. Yet when we put a hypodermic

needle into the trachea and inflated the fetal lungs with oxygen, even though these animals may have been delivered for a number of minutes, they responded to the oxygen, began to breathe, and survived.

In regard to the relation of intrauterine respiratory movements to aspiration of amniotic fluid, and the effect aspiration may have on later ability of the child to breathe, I should say that in our experiments those newborn fetuses which had aspirated the amniotic contents nearly always showed râles in the chest which we could hear quite easily.

We do not hold that aspiration is a normal phenomenon in utero, and I think we have some good evidence that it is not. The lung of a full-term guinea pig fetus removed after clamping the trachea in utero to prevent aspiration has a glandular appearance. The lung of one allowed to execute strong intrauterine respiratory movements is partly expanded by the aspirated amniotic fluid and looks like the usual pictures of human stillborn lungs. In the lung of an animal born normally and allowed to breathe only five minutes, one sees many compact unexpanded regions like the truly atelectatic lung of the apneic full-term fetus.

REACTIONS TO ESTROGENS

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IT IS generally assumed that only stilbestrol produces nausea and vomiting and that the use of the so-called natural estrogens (estradiol, estrone, and estriol) or their derivatives does not provoke these undesirable side reactions. In my belief such an assumption is erroneous. Several observers[1, 2] have noted that the acetylenic derivative of estradiol, ethynil estradiol, causes a high incidence of nausea and vomiting. In the reprints of the article by Shorr, Robinson and Papanicolaou on stilbestrol, the detailed data for each patient is tabulated (not presented in the article as published in the *J. A. M. A.*[1]). Seventeen of these patients were given natural estrogens (not including ethynil estradiol) in addition to the stilbestrol. Five of these 17 patients are listed by the authors as having undesirable side reactions after administration of estradiol benzoate or a preparation of mixed (estronelike) estrogens. One of these patients had nausea and a second had nausea and vomiting. In addition to the observations to be presented in this paper, the present author has noted nausea and vomiting in a patient following estradiol benzoate (2.0 mg.) and in 3 patients following estrone (2 after 20,000 I.U. and 1 after 5.0 mg. suspended in oil).

Studies have been made on the clinical effectiveness of various natural and stilbene estrogens. In the course of these studies, reactions (nausea and vomiting) have been observed to follow the administration of natural estrogens as well as after stilbene compounds. Observations on reactions following an esterified natural estrogen are presented in this communication and compared with those following two comparable stilbene compounds.

REACTIONS TO ESTRADIOL CARBETHOXYLATE

Thirty-nine menopausal patients have been treated with parenteral estradiol carbethoxylate* for a period varying from eight to twenty-four

*Furnished through the courtesy of Drs. C. O. Miller and C. H. Mellish of Lakeside Laboratories.

weeks. The doses ranged from 1.0 to 10.0 mg. and averaged 4.37 mg. for the whole series. These dosages are obviously larger than those commonly used in clinical practice. They are comparable, however, to the amounts of stilbene estrogens which have been used by various workers.

Five of these 39 patients complained of nausea (12.6 per cent) and two of nausea and vomiting (5.3 per cent) following one or more treatments, a reaction incidence of 17.9 per cent during therapy with estradiol carbethoxylate. It is apparent that the production of nausea and vomiting is not a characteristic peculiar only to the stilbene estrogens, since these reactions also follow the use of this esterified natural hormone.

COMPARISON OF REACTION INCIDENCE PRODUCED WITH NATURAL AND STILBENE ESTROGENS

The reaction incidence with estradiol carbethoxylate is similar to that produced by comparable doses of an esterified stilbene in our hands. In a series of 136 menopausal patients reported elsewhere[3] stilbestrol dipropionate* caused vomiting in 1.5 per cent of the patients and nausea

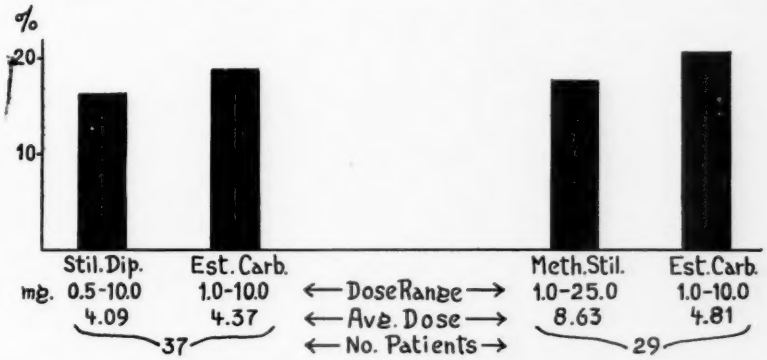

Fig. 1.—Reactions of patients to different estrogens.

(including those who vomited) in 14.7 per cent of the patients. In an incomplete study of the effectiveness of somewhat larger doses of methyl ether of stilbestrol,† data have been tabulated for 66 menopausal patients. Vomiting was produced in 3.0 per cent of these patients and nausea (including those who vomited) in 16.5 per cent of them.

A direct comparison of the natural and stilbene estrogens is possible since 37 of the patients given estradiol carbethoxylate had previously been treated with stilbestrol dipropionate. These patients were not selected; that is, no attempt was made to use only patients who had had no reactions to stilbestrol dipropionate. Estradiol carbethoxylate was given to successive patients whose necessary maintenance dosage of the stilbestrol dipropionate was judged to be established as accurately as is possible. This procedure was followed because our primary interest was to compare the clinical effectiveness of the two compounds.

In this group of patients there was little difference between the stilbestrol dipropionate and the estradiol carbethoxylate in the occurrence of reactions (Fig. 1). During the course of therapy with stilbestrol

*Furnished through the courtesy of Doctors C. O. Miller and C. H. Mellish of Lakeside Laboratories.

†Furnished through the courtesy of Dr. Franz Schmelkes of Wallace and Tiernan Products, Inc.

dipropionate 6 (16.2 per cent) of the 37 patients had nausea and 7 (18.9 per cent) complained of reactions following estradiol carbethoxylate.

Twenty-nine of these same patients were given methyl stilbestrol subsequent to their treatment with estradiol carbethoxylate. The reaction incidence was about the same for these two substances (Fig. 1). Six of these 29 patients (20.7 per cent) had had reactions following the estradiol carbethoxylate, and after methyl stilbestrol 5 (17.2 per cent) had reactions.

The dosage range and average doses of the 3 estrogens used in this procedure are shown in Fig. 1. The data for estradiol carbethoxylate are presented for the 37 patients who received stilbestrol dipropionate and are also recalculated for the 29 patients who also received methyl stilbestrol. Each different dose received by an individual is included in calculating the "average dose." It is evident that estradiol carbethoxylate was given in doses similar (in mg.) to those of the stilbestrol dipropionate and smaller than those of the methyl stilbestrol.

COMMENTS

These data are not presented with the intention of condemning the particular esterified natural estrogen used in this study. It seems probable that a similar reaction incidence would follow the use of *comparable effective amounts* of any other natural estrogen.

The average individual dose of estradiol carbethoxylate given to the 39 patients (4.37 mg.) according to Fischer's data[4] is equivalent to 13.15 mg. (131,500 I.U.) of estrone or 6.12 mg. (61,200 I.B.U., or 36,720 R.U.*) of estradiol benzoate. Judging from its clinical effectiveness the potency of estradiol carbethoxylate is somewhat less than this, but at any rate, the doses used in this study were at a level rarely approached in ordinary clinical practice.

There seems to have been little realization of the great potency of the doses of stilbestrol or related compounds used by many observers. It is difficult to express the potency of these compounds in terms of better known natural estrogens since various authors disagree in their determinations based on animal experiments. However, Shorr, Robinson and Papanicolaou[1] have presented data concerning the potencies of these various compounds in the human being. Calculating from their data, 1.0 mg. of parenteral stilbestrol has the same activity as 17,000 to 21,000 I.U. of parenteral estrone. To obtain the estrogenic effect of 5.0 mg. of stilbestrol one would have to give 85,000 to 105,000 I.U. of estrone in one single injection. The oral potency of stilbestrol is 50 to 100 per cent (average approximately 78 per cent) that of parenteral stilbestrol. The 2.0 to 4.0 mg. daily dose which these authors consider to be the "oral estrogenic unit" is therefore equivalent to the *daily injection* of somewhere between 26,000 and 63,000 I.U. of estrone.

The fact that reactions have not previously been associated to any great extent with the use of natural estrogens is understandable. These substances are very costly to prepare and have been furnished to the clinicians in dosage forms that are relatively minute when contrasted

*1 mg. = 6,000 R. U.

to those of stilbestrol and related compounds. The amounts in ordinary clinical usage are insufficient to cause such responses.

The toxic actions and pathologic changes which have been produced in experimental animals with stilbestrol have been mentioned in several clinical articles. The manner in which these references have been presented seems unfortunate to me. It is quite true that, if given in sufficient quantities, stilbestrol is capable of producing grave pathologic effects.[5-8] However, we believe it should have been emphasized that the doses necessary to produce these effects must be 3,000 to 3,000,000 times the physiologic dose in the animals concerned. Of even greater importance is the neglected fact that equally potent amounts of the natural estrogens are also toxic and cause similar pathologic changes.[9-15] These effects, therefore, are not peculiar to stilbestrol, but are characteristic of estrogens in general. The fact that tremendous overdoses of estrogens are capable of producing truly toxic effects in experimental animals is, however, not of clinical importance. There are few substances of therapeutic value which are not toxic when given in equally tremendous overdoses.

SUMMARY

An esterified natural estrogen, estradiol carbethoxylate, has been used in treating 39 menopausal patients. Thirty-seven of these patients had previously been given stilbestrol dipropionate. The incidence of undesirable side reactions was as high with estradiol carbethoxylate as with the stilbestrol dipropionate. Twenty-nine of these patients were given methyl stilbestrol subsequent to the estradiol carbethoxylate and showed approximately the same reaction incidence with both substances.

It is believed that nausea and vomiting are nonspecific responses which may be evoked by very high doses of natural as well as synthetic estrogens.

REFERENCES

(1) *Shorr, E., Robinson, F. H., and Papanicolaou, G. N.:* J. A. M. A. **113:** 2312, 1939. (2) *Loesser, A. A.:* Brit. M. J. **1:** 13, 1939. (3) *Greene, R. R., and Dorr, E. M.:* J. Clin. Endocrinol. In press. (4) *Fischer, A.:* Arch. internat. de pharmacodyn. et de thérap. **58:** 332, 1938. (5) *Varangot, J.:* Presse méd. **47:** 725, 1939. (6) *Loeser, A.:* Ztschr. f. d. ges exper. Med. **105:** 430, 1939. (7) *Arnold, O.:* Klin. Wchnschr. **18:** 1891, 1939. (8) *Tislowitz, R.:* Acta brev. Neerland. **9:** 15, 1939. (9) *Arnold, O., Holtz, F., and Marx, H.:* Naturwiss. **24:** 314, 1936. (10) *Selye, H.:* Canad. M. A. J. **41:** 48, 1939. (11) *Burenther, A., and Schabbel, E.:* Klin. Wchnschr. **16:** 1667, 1937. (12) *Balo, J. V., and Purjesz, B.:* Klin. Wchnschr. **16:** 1160, 1937. (13) *Tislowitz, R.:* Acta. brev. Neer. **8:** 103, 1938. (14) *Kochakian, C. D.:* Endocrinology **26:** 54, 1940. (15) *Greene, R. R., and Burrill, M. W.:* Unpublished observations.

Calero, Carlos M.: Menstruation During Pregnancy, Rev. de gynec. e. d'obst. (Rio de Janeiro) **2:** 69, 1940.

After reporting the medical history of a case, the author reviews the causes of hemorrhage during pregnancy. Going into details concerning all possible types of such hemorrhages including an analysis of chemic and cytologic changes in pregnant and menstruating women, he definitely concludes that the case presented is one of menstruation during pregnancy.

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GYNECOLOGIC SURGERY UNDER LOCAL ANESTHESIA

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LOCAL anesthesia has been used for many years in this country in gynecologic surgery. There are those[1-3] who have strongly advocated its use and have employed it with satisfactory results. Bartlett[4] found a mortality rate from ether anesthesia of 0.15 per cent, or one case in 738. Rollison[5] encountered six deaths in 6,062 patients receiving a general anesthetic, but no anesthetic deaths in 1,981 cases receiving local anesthesia. Moreover, local anesthesia has been found to produce fewer pulmonary complications, reduce dehydration and acidosis as well as gastrointestinal disturbances.

Spinal anesthesia has its advocates and in some hands it can apparently be used with great safety. However, those who have studied large series of cases from many clinics are of the opinion that operations performed under spinal anesthesia carry a definite hazard. Babcock,[6] for example, in a series of 215,000 patients receiving spinal anesthesia, recorded 75 anesthetic deaths, or one in 2,867 cases. Bower et al.[7] after a careful study stated that, "spinal anesthesia is responsible for more deaths than any other anesthetic in proportion to the number administered."

We, at the New York Hospital clinic, have likewise been impressed with the advantages of local anesthesia. We began by using it only in cases having definite medical complications. These results were so satisfactory that its use was extended to include many uncomplicated cases and elderly women. We have been repeatedly impressed by its relative safety and by an apparent decrease in morbidity, shock, and blood loss. These latter points have never been properly analyzed in previous papers, nor has the problem of the aged gynecologic patient been properly considered. With this in mind, we have analyzed our results with local anesthesia.

MATERIAL

This material was drawn from the records of the Gynecological Service of the Lying-in Hospital from January, 1936, to December, 1940, inclusive. These cases represent all the major gynecologic operations performed under local anesthesia from both the private and ward services during these years. The number of vaginal operations was 177, and the abdominal 23, a total of 200 cases (Table I). The control material consisted of 177 major vaginal and 100 major abdominal operations performed under general anesthesia. These were consecutive cases, but were limited so that the percentage of operations performed each year was the same for both types of anesthesia. This was necessary because the number of operations performed under local anesthesia steadily increased each year.

METHODS

Whether a vaginal or abdominal operation is to be performed, the following preliminary medication is administered: Pentobarbital sodium 0.1 Gm. the night before operation and 0.2 Gm. an hour and one-half prior to operation, supplemented by morphine sulfate 0.010 Gm. and scopolamine hydrobromine 0.0004 Gm. one hour later.

The technique for local pudendal and perineal block anesthesia is essentially that described by Urnes[8] (Fig. 1).

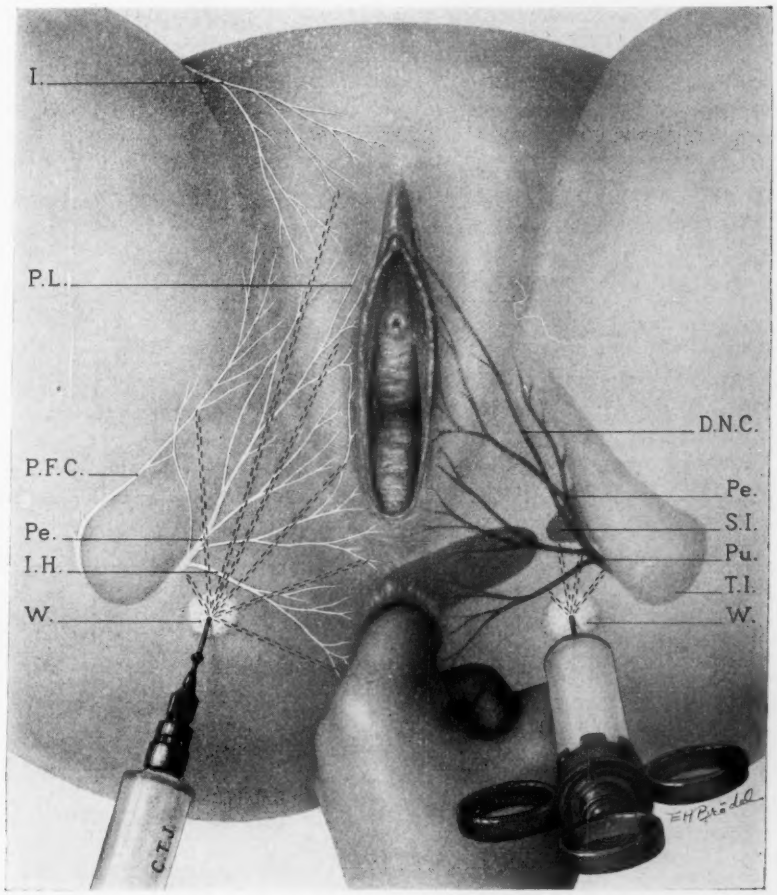

Fig. 1.—Diagram showing local infiltration technique of the nerves of the female perineum. Superficial and deep innervation is shown on the right and left sides of the patient, respectively. *I.*, Ilioinguinal nerve; *P.L.*, posterior labial nerve; *P.F.C.*, posterior femoral cutaneous nerve, perineal branch; *Pe.*, perineal nerve; *I.H.*, inferior hemorrhoidal nerve; *D.N.C.*, dorsal nerve of clitoris; *Pu.*, pudendal nerve; *S.I.*, spine of ischium; *T.I.*, tuberosity of ischium; *W.*, wheal, intradermal.

With the patient in the exaggerated lithotomy position, intradermal wheals are made bilaterally, halfway between the rectum and the tuberosity of the ischium. The anesthetic used is 0.5 per cent procaine. The index finger is inserted into the rectum to palpate the ischial spines. A 10 cm. needle is passed horizontally through the cutaneous wheal directly to the spine, and is allowed to slip just under and beyond it. Because of the direction of the needle and the guiding finger in the rectum, there is no danger of piercing the rectum. From 10 to 15 c.c. of solution is de-

posited at this point, blocking the internal pudic nerve as it passes dorsal to the spine of the ischium just before entering Alcock's Canal. The needle is then withdrawn until it lies just beneath the skin. The direction is then changed laterally toward the tuberosity of the ischium, and the needle is then inserted until the point strikes the bone. Five cubic centimeters are injected while the needle is gradually withdrawn. This anesthetizes the large perineal branches of the posterior cutaneous femoris. The needle is again withdrawn until it lies just beneath the skin and its direction is changed vertically upward. While it is advancing, 5 c.c. is deposited in the subcutaneous tissue of the labium majus, blocking off the perineal fibers of the ileoinguinal nerve.

TABLE I. LIST OF OPERATIONS

OPERATION	NO. CASES
General Anesthesia: A. Vaginal Operations	
Anterior and posterior repair	71
Manchester operation and posterior repair	78
Vaginal hysterectomy	7
Repair of fistula	2
Amputation of cervix and posterior repair	10
Watkin's interposition and posterior repair	2
Excision of cervix	1
Repair of hernia of cul-de-sac of Douglas	2
Vulvectomy	1
Anterior and posterior repair and laparotomy	3
Total	177
B. Abdominal Operations	
Hysterectomy and salpingo-oophorectomy	57
Panhysterectomy	2
Uterine suspension	16
Myomectomy	8
Oophorocystectomy and appendectomy	15
Exploratory laparotomy	2
Total	100
Local Anesthesia: A. Vaginal Operations	
Anterior and posterior repair	77
Manchester operation and posterior repair	75
Vaginal hysterectomy	1
Repair of fistula	4
Amputation of cervix and posterior repair	3
Repair of third degree laceration	1
Watkin's interposition and posterior repair	1
Excision of cervix	1
Repair, hernia cul-de-sac of Douglas	1
Vulvectomy	3
Le Fort	10
Total	177
B. Abdominal Operations	
Hysterectomy	2
Panhysterectomy	1
Oophorocystectomy	7
Tubal ligation	2
Exploratory laparotomy	10
Abdominal and vaginal	1
Total	23

"The procedure is repeated on the opposite side, the operator using the same finger of the right hand. The vaginal mucosa and skin of the perineal area as high as the clitoris becomes anesthetized in five minutes. Relaxation of the levator ani and perineal muscles is usually complete at this time."

Some operators prefer to locate the ischial spines per vaginam rather than rectally thereby avoiding the rectum as a source of contamination. One per cent procaine

is used in some instances instead of 0.5 per cent. In selected cases epinephrine is added to control bleeding and to prolong the anesthetic. To avoid injection of the solution into the blood stream, constant movement of the needle is necessary.

Anesthesia for abdominal operations is obtained by the systematic infiltration of a procaine solution in the skin of the abdominal wall beginning in the midline and extending laterally for a distance of 4 or 5 cm. After a period of three to five minutes, the skin and subcutaneous tissue to the fascia of the recti are incised. In a similar manner, the fascia is infiltrated and the muscle, if desired. The parietal peritoneum is infiltrated in the midline and to either side prior to incision, the thin filmy layers standing out in relief when the solution is gently injected. Further infiltration of the round, broad, and uterosacral ligaments and the visceral peritoneum may be carried out, depending on the extent of the operation. Two hundred to 300 c.c. of procaine is usually sufficient to produce a satisfactory anesthetic. Retractors should be avoided, tissues should be handled as gently as possible and packs should be used only when absolutely necessary.

ANESTHETIC RESULTS

We have attempted to evaluate the results of the anesthesia in the following manner: Grade 1, an entirely satisfactory result. Grade 2, a partially satisfactory result, the procaine affording satisfactory relief of pain for at least one hour but requiring an inhalation anesthetic thereafter. Grade 3, a failure.

We obtained Grade 1 anesthesia in 82.8 per cent (Table II) of the 177 major vaginal operations, 6.7 per cent Grade 2 results, and 10.1 per cent Grade 3, or failures, a result which compares favorably with Mathews,[9] who in 443 major and minor vaginal operations, obtained 70 per cent excellent results, 28 per cent good results, and 1.8 per cent failures. Gellhorn[1] also using the infiltration technique, rather than the pudendal block, obtained 64.5 per cent excellent results, 31.5 per cent good results, but requiring supplementary inhalation anesthesia, and 4 per cent failures in 82 cases of vaginal hysterectomy.

In 23 abdominal operations, we were able to obtain similar results to those obtained in vaginal operations, with 78.3 per cent, Grade 1, 13 per cent Grade 2, and 8.7 per cent failures. In both series, not a single instance of sensitivity to procaine was encountered.

TABLE II

Local Vaginal Operations (177 Cases)		
Anesthetic results:	Grade 1	82.8%
	Grade 2	6.7%
	Grade 3	10.1%
Local Abdominal Operations (23 Cases)		
Anesthetic results:	Grade 1	78.3%
	Grade 2	13.0%
	Grade 3	8.7%
All Local Operations (200 Cases)		
Anesthetic results:	Grade 1	82.5%
	Grade 2	7.5%
	Grade 3	10.0%

POSTOPERATIVE COMPLICATIONS

In the analysis of postoperative results, we have attempted to determine the mortality, morbidity, and other significant complications dur-

ing the convalescent period. By morbidity is meant a temperature rise to 38.0° C. (100.4° F.) on any two postoperative days excluding the day of operation, from the first to the tenth day, temperatures being taken orally every six hours.

TABLE III. POSTOPERATIVE COMPLICATIONS

LOCAL ANESTHESIA		GENERAL ANESTHESIA	
Vaginal Operations (177 Cases)		*Vaginal Operations (177 Cases)*	
Febrile	22.5%	Febrile	32.2%
Postoperative shock	7.9	Postoperative shock	17.6
Urinary tract infection	13.6	Urinary tract infection	13.0
Respiratory infection	3.9%	Respiratory infection	1.2%
Deaths (1)		Deaths (0)	
Abdominal Operations (23 Cases)		*Abdominal Operations (100 Cases)*	
Febrile	39.1%	Febrile	43.0%
Postoperative shock	4.3	Postoperative shock	4.0
Urinary tract infection	8.7	Urinary trace infection	1.0
Respiratory infection	8.7%	Respiratory infection	7.0%
		Deaths (1)	
Total Cases (Abdominal and Vaginal: 200 Cases)		*Total Cases (Abdominal and Vaginal: 277 Cases)*	
Febrile	24.5%	Febrile	36.1%
Postoperative shock	7.5	Postoperative shock	12.6
Urinary tract infection	13.0	Urinary tract infection	8.7
Respiratory infection	4.5%	Respiratory infection	3.2%
Deaths (2)		Deaths (1)	

There were three deaths (Table III) in the entire series. Of these, only one could be attributed to the anesthetic, which was in this particular case, gas-oxygen-ether. This patient died on the operating table, apparently of respiratory collapse, directly after opening the abdomen. The two other deaths occurred during the convalescent period and were in patients in whom local anesthesia had been used. There is, however, no evidence to indicate that either of these deaths were associated with the anesthetic agent. One patient died on the second postoperative day of advanced carcinomatosis and heart disease, the other died on the fourteenth postoperative day following a pulmonary embolus after an afebrile course.

CASE REPORTS

CASE 1.—(No. 157934). The patient was a 35-year-old colored female admitted to the Lying-in Hospital with a diagnosis of myoma uteri. Her general physical examination was entirely normal. Blood pressure was 140/90, with the cardiac findings otherwise not remarkable. A supravaginal hysterectomy was recommended. After routine preoperative analgesia of morphine and atropine, the anesthetic was begun. Nitrous oxide-oxygen mixture, administered by the closed method was used for the induction, this being supplemented by ether. The operation had proceeded as far as division of the round ligaments and clamping of the uteroovarian ligament on one side, when respirations ceased. Artificial respiration and stimulants produced no response. She received a total of 30 c.c. of ether, the duration of the anesthetic being forty-two minutes, the operating time fifteen minutes. The clinical cause of death was nitrous oxide-ether narcosis with respiratory collapse. Autopsy was obtained and showed no significant lesions.

CASE 2.—(No. 260072). The patient was a 70-year-old, white woman who was admitted to the Gynecological Service with a diagnosis of probable carcinoma of the ovary. She presented, in addition, hypertensive cardiovascular disease (blood pressure 180/100) and a microcytic hypochromic anemia (hemoglobin 7.0 Gm.). Medical consultation was obtained and although the patient was considered to be a poor operative risk, laparotomy under local anesthesia for the investigation of the pelvic mass was deemed advisable. A blood transfusion was given preoperatively and preoperative medication included pentobarbital sodium 0.1 Gm., morphine sulfate 0.010 Gm., and scopolamine hydrobromide 0.0003 Gm. Procaine 1 per cent was used for infiltration of the anterior abdominal wall. The pathology was found to be an advanced ovarian malignancy and after biopsy of a small portion of the omentum, the incision was immediately closed. The operation lasted forty minutes, and the patient's condition was good throughout. The patient's course was steadily downhill after the first day postoperative. While receiving a transfusion on the second day, the patient died. The blood was rematched and was found to be compatible. Death was considered to be due clinically to heart failure. Autopsy confirmed the findings of advanced serous cystadenocarcinoma of the ovary with multiple metastases together with thrombi in the right auricle and ventricle.

CASE 3.—(No. 260750). The patient a 62-year-old, Jewish housewife, was admitted to the Gynecological Service with a diagnosis of cystocele, rectocele, and hypertensive cardiovascular disease. Blood pressure was 160/110. The remainder of the physical and laboratory studies were not remarkable. A dilatation and curettage, cervical polypectomy and an anterior and posterior colporrhaphy were performed, using 1 per cent procaine, local pudendal block anesthesia. The patient withstood the procedure well. On the day of operation, the temperature rose to 38.0° C., this being the only day on which she had fever. She was allowed out of bed on the morning of the fourteenth postoperative day without apparent ill effects. During that afternoon, she was again allowed up, and while standing beside her bed, she collapsed. Routine stimulants and artificial respiration were of no avail and the patient died within fifteen minutes. The clinical cause of death, confirmed by autopsy, was pulmonary embolus originating from a pelvic thrombophlebitis.

The morbidity rate in the group of patients operated upon under local anesthesia was 24.5 per cent, as compared with 36.1 per cent for those patients receiving general anesthesia (Table III). This reduction in morbidity is all the more significant when it is realized that those patients receiving procaine anesthesia were poorer risks than those operated upon under general anesthesia.

The number of patients developing postoperative shock was substantially decreased by local anesthesia, 7.5 per cent developing shock as compared with 12.6 per cent in the general group. This may be partially explained by a decrease in blood loss although the actual measurement of blood was not carried out.

Respiratory disease occurred postoperatively in 4.5 per cent of those patients receiving local as compared with 3.2 per cent of those receiving general anesthesia. The incidence of respiratory disease preoperatively, however, was 12.5 per cent in the former but only 2.5 per cent in the latter.

PREOPERATIVE COMPLICATIONS

Any consideration of postoperative morbidity and mortality must be interpreted in the light of the preoperative condition of the patient. Hypertensive cardiovascular disease was found in 45.7 per cent of the patients having vaginal operations under local, but in only 5.8 per cent of those receiving a general anesthetic (Table IV). This diagnosis was corroborated in each incidence by a medical consultant. Similarly, the other forms of heart disease were likewise more frequent in the former group. Diabetes was noted in 8.5 per cent of the patients receiving procaine while being present in 1.69 per cent of the general vaginal patients. Respiratory disease occurred in 12.9 per cent of the former and 2.25 per cent of the latter. Urinary tract disease was not a common finding in these patients preoperatively, for it was not observed in a single patient receiving a general anesthetic and in only 2.8 per cent of the other group.

TABLE IV. PREOPERATIVE COMPLICATIONS

	HYPERTENSIVE CARDIO-VASCULAR DISEASE	OTHER CARDIAC DISEASE	BLOOD PRES-SURE 140/90 OR +	RESPIR-ATORY DISEASE	DIABETES	ANEMIA
General abdominal (100 cases)	4.0%	1.0%	10.0%	3.0%	5.0%	2.0%
General vaginal (177 cases)	5.8	0.56	20.3	2.25	1.69	1.68
Local abdominal (23 cases)	34.7	13.0	60.8	8.6	4.3	8.6
Local vaginal (177 cases)	45.7%	4.5%	61.0%	12.95%	8.5%	1.12%

THE AGED PATIENT

It has been shown that the life expectency of the general population has steadily increased, necessitating, therefore, the care of patients of more advanced years. Recent releases from the Bureau of Census based on the 1940 decennial census reveals[10] that, "The median age of the population of the United States increased to 28.9 years in 1940, from 26.4 years in 1930. Furthermore, the persons 65 years of age and over now number 8,956,000, an increase of 35 per cent over the number in this group in 1930." Through the medium of local anesthesia, we have been able to reduce the risk of operative complications in aged individuals. In recent years, we have operated upon many elderly women whom previously we should have turned away as too great risks. The average age of the patients operated upon under local anesthesia was 53 years, while those of the control group averaged 41.5 years (Table V).

TABLE V

OPERATIONS	CASES	AVERAGE AGE
General abdominal	100	35.84 years
General vaginal	177	44.7 years
Local abdominal	23	47.2 years
Local vaginal	177	53.8 years
Average age for group: 46.4 years.		
Average age for all locally anesthetized patients: 53.0 years.		
Average age for all generally anesthetized patients: 41.5 years.		

It is of interest that we found a total of 57 patients over 60 years of age, 7 of these having passed 70, all operated upon under local anesthesia without a single anesthetic death and with a morbidity rate of but 12.7 per cent.

SUMMARY

1. A total of 200 major gynecologic operations were performed without reaction to procaine.

2. In the same series, there were two deaths during the postoperative period, neither attributable to the anesthetic agent.

3. In a control series operated upon under general anesthesia, there was one anesthetic death considered due to nitrous oxide-ether narcosis.

4. The morbidity rates for the local and general anesthesia series were: 24.5 per cent and 36.1 per cent, respectively.

5. Postoperative shock was reduced from 12.6 per cent using general anesthesia to 7.5 per cent using local.

6. Respiratory infections occurred postoperatively in 4.5 per cent of the local group as compared with 3.2 per cent of the general series. However, the incidence of respiratory disease in the former was 12.5 per cent and 2.5 per cent for the latter preoperatively.

7. Urinary tract disease occurred postoperatively in 13.0 per cent of patients receiving procaine anesthesia as against 8.7 per cent of those receiving general anesthesia. However, 3.5 per cent of the local group had urinary tract pathology prior to operation, but none of the patients operated upon under general anesthesia were so affected.

8. The average age of patients operated upon under local was 53.0 years, while those of the control group averaged 41.5 years.

9. Fifty-seven patients over 60 years of age were operated upon, using procaine anesthesia, without an anesthetic death, and with a morbidity rate of 12.7 per cent.

CONCLUSIONS

Any type of gynecologic vaginal operation can be satisfactorily performed under perineal-pudendal block local anesthesia with reduction of the mortality and morbidity. Gynecologic abdominal surgery performed under local anesthesia, while less satisfactory in general, may be used advantageously in selected cases.

Local anesthesia by its safety has extended the scope of surgery and is the method of choice for anesthesia in the elderly woman.

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REFERENCES

(1) *Gellhorn, G.:* J. A. M. A. **61:** 1354, 1913; Surg., Gynec. & Obst. **45:** 105, 1927; Ibid. **51:** 484, 1930. (2) *Greenhill, J. P.:* J. A. M. A. **102:** 28, 1934. Inter. Clin. **4:** 171, 1925. (3) *Fall, F. H.:* Am. J. Obst. & Gynec. **3:** 400, 1922; **20:** 310, 1930. (4) *Bartlett, M. K., and Simmons, F. A.:* Surg., Gynec. & Obst. **55:** 777, 1932. (5) *Rollison, J. W.:* M. J. Australia **2:** 580, 1929. (6) *Babcock, M. E.:* Anesth. & Analg. **11:** 184, 1932. (7) *Bower, J., Clark, J. H., and Burns, J. C.:* J. A. M. A. **100:** 245, 1933. (8) *Urnes, M., and Timmerman, J.:* Ibid. **109:** 1616, 1937. (9) *Mathews, H. B., and Mazzola, V. P.:* N. Y. State J. Med. **37:** 1, 1937. (10) Editorial, J. A. M. A. **116:** 1526, 1941.

TWIN PREGNANCIES IN THE SERVICE OF THE CHICAGO LYING-IN HOSPITAL

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TWINS are of perennial interest not only to the obstetrician who delivers them but also to the embryologist, geneticist, or any scientist who may have an opportunity to observe them. The obstetrician is well aware of the dangers to the fetus and the increase in maternal complications which frequently occur with multiple pregnancies. The present series covering a period of ten years furnishes additional data on the probability of premature birth, maternal complications, and fetal and neonatal death.

From the opening of the present Chicago Lying-in Hospital May 25, 1931, until Jan. 1, 1941, there were 25,583 women delivered in the hospital and 5,548 by the Home Service Department. Among those in the hospital there were 281 who had twin pregnancies, and 2 who had triplets; of the home deliveries 52 had twins, none triplets. This is an incidence of 1:91 for twins among women in the hospital, 1:106.6 for women delivered at home, and 1:93.4 for the total 333 twin pregnancies. The incidence is slightly lower than that for the country as a whole. In the United States registration area, approximately one in every 87 pregnancies results in a multiple birth.[1]

Three of the mothers in the hospital and one mother at home delivered one reportable infant and one whose size and weight placed it in the nonreportable group (abortions). In addition, one patient had one fetus in the uterus and one in the Fallopian tube. Since the conditions surrounding the fetus in utero were those of a single pregnancy this case is omitted from the following discussion, and the figures are based on 332 twin pregnancies with 660 reportable infants.

A complete record of the incidence of twins among abortions in which the larger fetus weighed less than 400 Gm. is not available. Among approximately 1,200 abortions, however, there are one known set of triplets and at least 12 pairs of twins.

Previous Pregnancies.—Only 29.6 per cent (98) of the women in this series were primigravidas, in comparison to 42 per cent of primigravidas among the total number of women delivered at home and in the hospital during the same period. The remaining 70 per cent of patients with twins were distributed as follows: second pregnancy 25.3 per cent (84), third pregnancy 19.2 per cent (64), fourth pregnancy 8.1 per cent (27), and in the fifth to eleventh pregnancies 17.8 per cent (59). The average number of previous pregnancies was 1.89 for all patients with an average of 0.31 (16.5 per cent) of these ending in abortions. The 104 abortions occurred among 92 women, only 27.7 per cent of those in this series having had one or more pregnancies which terminated in this manner.

Two women had successive sets of twins, one in the first and second pregnancies, one in the seventh and eighth pregnancies, both of which are included in this series; two had twin pregnancies which were not successive (second and fourth, and unknown and ninth) and only one set of each is included. In most instances a definite history of the occurrence of twins among the relatives of the patient is lacking. In the triplet abortions, not included in this series, the siblings of the patient include two sets of twins.

Birth Weight.—The State of Illinois requires registration of all births and stillbirths in which the infant is advanced to the fifth month of gestation. Since the calculated gestational age is often inaccurate if based only on menstrual history, it seems more desirable to use a classification including weight and length in addition to menstrual age. All babies born in this hospital are grouped according to these three criteria, and this classification, having been given in several previous publications,[2-4] will not be repeated. Since practically all infants born before the end of the seventh lunar month fail to survive (weight at this time about 1,000 Gm.) these infants are separated into a special group which must be reported in mortality statistics even though they cannot be expected to live. An average of 35 per cent of those between 1,000 Gm. and 1,500 Gm. will survive, and it does not seem justifiable to consider, as do many authors, 1,500 Gm. as the lower limit of viability. In this paper those below 400 Gm. are considered as abortions, 400 to 1,000 Gm. as previable; 1,000 to 2,500 Gm. as premature and those over 2,500 Gm. as at term. Forty-three and six-tenths per cent of the twins were premature in contrast to 5.83 per cent of single pregnancies, and 5.2 per cent were previable in contrast to 0.52 per cent of single pregnancies occurring in this hospital. In his series of 503 twin infants over 1,500 Gm., Guttmacher[5] states that 56 per cent were of term weight, 44 per cent premature, but over 1,500 Gm. In the present series 53.3 per cent of the twins over 1,500 Gm. weighed over 2,500 Gm.

Dividing the twins into those delivered in the hospital and at home, it is interesting to note the higher incidence of infants weighing more than 2,500 Gm. among those delivered at home; in the latter group 64.5 per cent were over 2,500 Gm., in those delivered in the hospital only 49.4 per cent.

The average birth weight of 1,000 single infants delivered in this hospital was 3,405 Gm.; for this entire group of twins the average weight was 2,391 Gm., the latter having a birth weight only 70 per cent as great as that of an infant which has not shared the uterine cavity with another. Among these 1,000 infants, the average birth weight of those in which the length of gestation was considered as being at term (767 infants with a period of gestation of 265 to 295 days) was 3,418 Gm.; the average birth weight of twins at term (219 infants) was 2,706 Gm., the latter being 82 per cent of the former. The difference between 70 per cent in all pregnancies and 82 per cent in infants delivered within two weeks of term is accounted for by the greater incidence of the premature onset of labor among twin than among single pregnancies. The average weight together with the degree of variability and the percentage of cases falling in each group are shown in relation to the length of gestation in Table I. Daiser[5] in his group of 489 twins found that twins tended to weigh more than single fetuses until about the two hundred and thirty-fifth day of gestation, during the next two weeks they were about equal in weight, and from then on until 280 days the weight of the twins was proportionately less. This was not borne out in the present series, the twins having a consistently lower mean weight than that of the single fetuses of corresponding gestational age.

In 118 pregnancies both infants were at term according to weight; the one weighed more than 2,500 Gm. and the other between 1,000 and 2,500 Gm. in 83; one weighed over 2,500 and the other less than 1,000 in 3; and one was at term, the other an abortion in one case. In 102 pregnancies, both were in the premature weight group, in 13 both were previable, in 2 one was in the premature, the other in the previable group, in 3 one was in the previable group, the other in the group of abortions. In 2 cases each, one infant was at term and the weight of the other unrecorded, one was premature and the other unrecorded, and in 4 the weights of both infants were unrecorded. The total infants at term numbered 325, premature 290, previable 34, abortions 4, unrecorded 11.

The average difference between the weights of the 2 fetuses is shown in Table II. When the larger fetus weighs between 2,000 and 3,500 Gm., the smaller fetus weighs about 12 per cent less. In fetuses weighing less than 2,000 Gm., the difference is proportionately somewhat less, in fetuses over 3,500 Gm. the difference is somewhat greater.

Of reportable twin infants, 49.4 per cent were at term according to weight in contrast to 94.8 per cent which were at term among 1,000 unselected single infants from this hospital.

TABLE I. WEIGHT IN RELATION TO LENGTH OF GESTATION

LENGTH OF GESTATION FROM FIRST DAY OF LAST MENSTRUAL PERIOD	SINGLE PREGNANCIES 1,000 CASES			TWIN PREGNANCIES 332 CASES		
	PREG. %	MEAN WEIGHT	COEFFICIENT OF DEVIATION	PREG. %	MEAN WEIGHT	COEFFICIENT OF DEVIATION
Total pregnancies	100	3405.8	157.2	100	2391.5	204.9
Term (265-295 days)	77.55	3418.3	140.6	52.81	2706.0	107.1
200-209	----	----	----	2.15	1650.0	139.5
210-219	----	----	----	2.33	1565.3	196.9
220-229	0.7	2716.6	152.3	5.57	2157.1	136.5
230-239	0.6	2050.0	238.0	7.36	1900.0	281.9
240-249	1.92	2923.6	121.1	10.05	2300.9	299.5
250-259	2.43	3133.3	180.2	14.54	2388.7	144.5
260-269	9.5	3098.9	142.7	19.56	2553.7	124.7
270-279	27.4	3325.0	136.9	25.68	2724.6	137.7
280-289	31.85	3591.0	122.3	10.59	2767.2	143.3
290-299	19.21	3618.6	131.6	2.16	2975.0	193.4
300-309	4.15	3650.0	110.8	0	0	----
310-319	1.84	3556.0	104.8	0	0	----
320+	0.40	3777.0	130.4	0	0	----

TABLE II. LENGTH OF GESTATION IN RELATION TO WEIGHT AT BIRTH

WEIGHT IN GRAMS	SINGLE PREGNANCIES			TWIN PREGNANCIES				
	PREG. %	MEAN LENGTH OF GESTATION	COEF. OF DEV.	PREG. %	MEAN LENGTH OF GESTATION	COEF. OF DEV.	AV. DIF. IN WEIGHT OF FIRST AND SECOND TWIN*	COEF. OF DEV.
Total pregnancies	100.0	281.7	12.4	100.0	256.2	25.4	--	--
Term (over 2,500 Gm.)	94.8	282.4	12.5	47.3	268.8	13.3	--	--
1-499	0.0	--	--	1.2	--	--	--	--
500-999	0.0	--	--	4.7	--	--	--	--
1,000-1,499	0.2	--	--	5.2	225.7	8.3	--	--
1,500-1,999	0.4	243.7	11.4	15.6	246.6	6.6	162.5	30.0
2,000-2,499	3.6	259.4	15.1	25.9	258.6	5.3	278.6	199.5
2,500-2,999	14.2	275.6	14.9	32.0	267.3	12.7	322.8	280.6
3,000-3,499	41.5	282.8	12.9	13.9	271.1	13.9	437.7	100.2
3,500-3,999	30.1	285.2	11.6	1.5	281.4	6.4	825.0	299.0
4,000-4,499	8.7	287.2	11.3	--	--	--	--	--
4,500 or over	1.3	292.1	5.4	--	--	--	--	--

*The larger of the two infants determined the grouping.

Length of Gestation.—Calculated from the first day of the last menstrual period the average length of gestation in the 1,000 unselected single pregnancies mentioned above was 281 days. The average length of gestation in all of the twin pregnancies was 256 days. There is a much greater variation in the length of gestation in twin than in single pregnancies. Seventy-seven per cent of the single infants were delivered within fifteen days of the calculated term date (265 to 295 days from the

first day of the last menstrual period). Among twins only 52.8 per cent were delivered within this same period. The majority of twins (87 per cent) were delivered before 280 days while less than half of single infants were delivered before the same date.

The average length of gestation for infants in single pregnancies in which the birth weight was within the range considered as normal for an infant at term (2,500 to 4,500 Gm.) was 282.4 days. The average length for infants in twin pregnancies for the same weight group was 268.8 days, or an average of fourteen days less than in single pregnancies. Part of this may be accounted for by the proportionately greater number of twin infants in the lower weight groups, but when they are divided into 500 Gm. groups, the average length of gestation is slightly shorter in twins in all of those over 2,000 Gm. (Table II). This suggests that these fetuses would have been greater than the average weight for single fetuses had pregnancy proceeded to term.

Sex Ratio.—The infants were of the same sex in 214 pairs of twins and of the opposite sex in 118 (female born first in 59, male born first in 59). Among those who were of the same sex 94 were females and 120 males. A total of 306 infants were of the female sex; 358 were male.* The ratio of female to male infants in total births according to the United States Bureau of Vital Statistics,[1] is 100:105; in this series of twins the ratio is 100:117.

Placenta.—Double placentas were recorded as occurring in 162 pregnancies, single or fused in 156, with no record in 15. In 71.1 per cent of the fused placentas and 58.5 per cent of the double placentas, the twins were of the same sex.

The average ratio between the placenta and the infant birth weight is similar to that generally considered normal for single pregnancies which according to Adair and Thelander[6] averages 1:7.1. The smaller the infant the lower the ratio and this doubtless accounts for the ratio in this series of twins. In the cases where the placenta was double, the average ratio was 1:6.7, where the placenta was single 1:6.5, and in the combined group 1:6.64. Adequate statements as to conditions of the fetal membranes are available only in the recent records. Among 10 of the dichorionic and 5 of the monochorionic single placentas, the infants were of the same sex; in 9 of the dichorionic and 1 of the monochorionic single placentas, they were of opposite sex. It is interesting that of 15 pairs of twins in this group, in only one were both infants female.

Position.—Both twins were in a cephalic position in almost half (159) of the total pregnancies. They were both breech in 25, while in 85 the first was cephalic, the second breech and in 33 the first was breech, the second cephalic. In 19, one twin was in a transverse position, scapula, etc., and in 11 the position of one or both was unrecorded. There are almost twice as many second infants in a breech position at the onset of labor as there are first infants (Table III); the great majority of the unusual presentations, especially scapula, are also found among second twins.

TABLE III. POSITION OF TWIN FETUSES AT THE ONSET OF LABOR

POSITION	FIRST TWIN	SECOND TWIN	TOTAL	PER CENT
Cephalic	261	194	455	68.5
Breech	63	114	177	26.6
Other	2	16	18	2.7
No record	6	8	14	2.2
Total	332	332	664	

Method of Delivery.—The type of delivery is shown in Table VI. It is interesting to compare these figures with those obtained from a study of all hospital and home deliveries occurring during the same period. Among the 31,131 deliveries in that series natural cephalic deliveries occurred in 66.5 per cent of the cases, among this series of twins in only 29.5 per cent; low or midforceps in 24.4 per cent,

*The sex of the 4 abortions is included.

among twins in 15.3 per cent; breech delivery in 3.2 per cent, among twins in 25.1 per cent; version and extraction in 0.8 per cent, among twins in 17.5 per cent; cesarean section in 4.5 per cent, among twins in 6.6 per cent. Of the total 256 versions and extractions, 115 (45 per cent) were performed for the delivery of second twins.

Mortality in Relation to Time of Death.—Among the 332 twin pregnancies, there were 28 (8.4 per cent) mothers who had neither baby living ten days after confinement, 36 (10.8 per cent) who had only one, and 268 (80.8 per cent) who had two living. There was a total mortality among the 664 offspring of 13.8 per cent (92), divided into 56 (59.8 per cent) neonatal deaths, 32 (35.9 per cent) stillbirths and 4 (4.3 per cent) abortions. These were divided into first and second twins as shown in Table IV.

TABLE IV. MORTALITY IN RELATION TO TIME OF DEATH

Stillbirths:	
Both stillborn	6
First living; second stillborn	12
Second living; first stillborn	7*
Neonatal deaths:	
Both died	16
First living; second died	12
Second living; first died	5
Neonatal death and stillbirth:	
First died; second stillborn	4*
Second died; first stillborn	2

*Includes two abortions (stillbirths).

The total mortality for the first born of twins is 12.0 per cent (25 neonatal deaths, 15 stillbirths), for the second born 15.6 per cent (30 neonatal deaths, 22 stillbirths). If, however, only the viable, nonmacerated fetuses and infants are considered, the mortality rates for first and second twins are almost identical as there are 21 such first born twins and 22 second born twins.

Mortality in Relation to Weight.—The total mortality among twins in which at least one twin had reached a reportable age was 13.8 per cent (Table V); this is over three times the mortality for total pregnancies which, during the same period, was 4.3 per cent. The higher total mortality rate is due to the larger number of previable fetuses and the greater proportion of viable premature infants than is found in the total deliveries. The general mortality for infants weighing over 2,500 Gm. is 1.9 per cent and for twins is slightly higher (2.4 per cent). The total hospital rate, however, for the viable premature infants (1,000 to 2,500 Gm.) is almost twice (32.6 per cent) that for twins of similar weight (19.6 per cent). This is largely accounted for by the greatly decreased incidence of stillborn fetuses in this weight group (15.2 per cent of all infants, 5.5 per cent of twins), although there is also a slightly lower incidence of neonatal deaths (17.4 per cent of all

TABLE V. MORTALITY IN RELATION TO WEIGHT

WEIGHT IN GRAMS	TOTAL BIRTHS	NEONATAL DEATHS	STILLBIRTHS	TOTAL NUMBER	MORTALITY PER CENT
2,500 and over	325	6	2	8	2.4
2,000-2,499	175	1	5	6	3.4
1,500-1,999	83	9	5	13	15.4
1,000-1,499	32	17	6	24	75.0
400- 999	34	20	14	34	100.0
Under 400	4	1	3	4	100.0
No record	11	1	2	3	
Total	664	55	37	92	13.86

infants, 14.1 per cent of twins). Of the infants weighing less than 1,500 Gm., 25 per cent survived. In his group of twins Goecke[7] reports 10.3 per cent of those in this group survived to the tenth day.

Among the 64 pregnancies in which one or both twins died or were stillborn, 50 were of the same sex (21 female, 29 male) and 14 were of the opposite sex. In 26 the placenta was double, in 36 it was single or fused, and in 2 there was no record. Death occurred to one or both twins slightly more frequently (23.0 per cent) when the placenta was single than when it was completely double (16.0 per cent).

Mortality in Relation to Method of Delivery.—The mortality among twins in relation to the method of delivery is difficult to compare with mortality in single pregnancies because of the greater incidence of prematurity in the former group, a condition which necessarily increases the number of deaths regardless of the type of delivery. Of greatest significance is the variation in the figures for version and extraction, the mortality among twins (8.6 per cent) delivered by this method being less than one-fourth that of all infants and fetuses delivered (34.5 per cent) in a similar fashion (this figure includes twins) (Table VI). The lower incidence is probably attributable (1) to the fact that when the operation is performed for the delivery of a single infant, it is done only in the presence of severe complications which in themselves greatly endanger the life of the fetus and (2) to the fact that it is a much more difficult technical procedure than when performed on the second twin. In the latter case the uterus is relaxed and one infant has already passed through the birth canal so that the operation itself presents relatively little difficulty.

TABLE VI. MORTALITY IN RELATION TO METHOD OF DELIVERY

METHOD OF DELIVERY	NUMBER OF BIRTHS		STILLBIRTHS AND NEONATAL DEATHS		
	FIRST TWIN	SECOND TWIN	WEIGHT UNDER 1,000 GM.	WEIGHT OVER 1,000 GM.	PER CENT MORTALITY OVER 1,000 GM.
Cephalic					
Natural	137	58	14	18	9.9
Low forceps	87	15	0	4	3.9
Mid or high forceps	14	4	0	1	5.5
Version and extraction	1	115	1	9	8.3
Breech	62	105	14	17	11.6
Cesarean section	22	22	2	1	2.2
No record	9	13	7	4	18.1
Total	664	92	38	54	8.6

Mortality in Relation to Anatomic State of Infant.—Over half of the dead infants and fetuses failed to show abnormalities at post-mortem examination (Table VII). Intracranial hemorrhage was present in 6, evidence of interference with umbilical circulation in 17, pneumonia in 6, and malformations in 6. Only 4 of the latter were believed to have died of the malformations.

Malformations are present in a much higher proportion of all twins including those that survive, than of single pregnancies, the incidence among total twins in this series being 2.8 per cent. This lends support to the belief that an abnormal intrauterine environment may in some cases be responsible for the abnormality. In only three instances were similar abnormalities found in both twins. These were 2 infants with umbilical hernias, 2 infants with cavernous hemangiomas of the anterior abdominal wall, one having, in addition, another hemangioma of the leg, and a third pair of infants in both of whom a diagnosis of congenital heart disease was made at two and twelve months, respectively. Among the infants who died, the malformations were all found in one twin of each pair. They were hydrocephalus, anencephalus, cleft palate and harelip, clubhand, mongolism, and congenital heart disease. Among those who survived there were harelip and cleft palate (present twice), hemangioma of lip, umbilical hernia, 6 fingers and toes, hypospadias, and hydrocephalus.

TABLE VII. CAUSE OF DEATH IN RELATION TO WEIGHT

CAUSE OF DEATH	FIRST TWIN		SECOND TWIN		TOTAL	
	STILLBORN	NEONATAL DEATH	STILLBORN	NEONATAL DEATH		
Over 2,500 Gm.						
No abnormality—fresh		2	1		2	
No abnormality—macerated					1	
Intracranial hemorrhage				3	3	
Anoxemia		1			1	
Pneumonia				1	1	
Malformations	1			1	2	10
1,000 to 2,500 Gm.						
No abnormality—fresh	1	7	2	8	18	
No abnormality—macerated	2		7		9	
Intracranial hemorrhage	1	1		1	3	
Anoxemia	2	4	2	2	10	
Pneumonia		1		1	2	42
Under 1,000 Gm.*						
No abnormality—fresh	4	8	1	8	21	
No abnormality—macerated	2		2		4	
Ruptured liver		1			1	
Anoxemia	1	1	1	3	6	
Pneumonia	1		2		3	
Malformations	1			1	2	37
No record of weight			2	1	3	3
Total	16	26	20	30		92

*Includes 4 abortions.

Adair[7] in 1930 reviewed the incidence of malformations in association with the birth of twins in the preceding 25,000 deliveries at the Chicago Lying-in Hospital. The incidence of twin to single pregnancies was about 1:70 with malformations occurring in only 1 per cent of the twin infants. In no instance were both twins of the pair malformed.

Maternal Complications.—Some abnormal state was present during pregnancy in 34.0 per cent (113) of the mothers bearing twins (Table VIII). The most common complication was pre-eclamptic toxemia (62), but the incidence of eclampsia was much higher than it was among women with a single fetus. The incidence of

TABLE VIII. MORTALITY IN RELATION TO MATERNAL COMPLICATIONS

	TOTAL MOTHERS WITH COMPLICATIONS	MOTHERS WITH 1 OR MORE DEAD INFANTS OR FETUSES	NUMBER OF FETAL AND NEONATAL DEATHS
Toxemia	62	7	8
Eclampsia	9	1	1
Hypertension	7	2	2
Nephritis	1	1	2
Placenta previa	4	3	6
Syphilis	3	0	0
Hydramnios	5	2	4
Pyelitis	2	0	0
Anemia	13	0	0
Cardiac	4	0	0
Hyperthyroid	2	0	0
Gaucher's disease	1	1	1
Total	113	17	24

eclampsia, 2.7 per cent, approximates closely that of other reports. Combining his figures with those of several other authors, Guttmacher[8] found an incidence of 2.79 per cent in 1,288 twin pregnancies. Goecke[9] reported 2.3 per cent in 131 cases. The total women in this series with pre-eclamptic, eclamptic, and hypertensive toxemia number 78, an incidence of 23.5 per cent. This is over 3 times the general incidence found by Dieckmann and Brown[10] at the Chicago Lying-in Hospital. It is difficult to compare these figures with those reported by other writers because of the varying criteria used in making a diagnosis of toxemia. However, McClure[11] found an incidence of 40 per cent pre-eclampsia and eclampsia in 165 cases. Guttmacher[8] had 35.3 per cent of late pregnancy toxemia, which was roughly two and one-half times the incidence in all pregnancies at the Johns Hopkins Hospital. Goecke[9] reports a 35 per cent incidence of hydrops, nephropathia, pre-eclampsia and eclampsia in a series of 131 twin pregnancies.

It is interesting that of the 11 fatalities in this group among infants born of mothers with some form of toxemia in only one pregnancy did both twins die. In this instance, one of the infants was malformed, the other died of intracranial hemorrhage following a version and extraction. In the other 9 women, only one twin died; if the toxemia produced direct detrimental effects on the fetuses which resulted in death, as it is commonly believed to do, one would have expected a similar effect on both twins. It suggests that death is coincidental rather than a direct result of the toxemia.

There were 7 mothers with essential hypertension, 2 of whom lost one baby each. In one of these there was a prolapsed cord, in the other polyhydramnios. Of the two mothers with nephritis, one delivered 2 stillborn fetuses, each weighing less than 1,200 Gm. while both of those from the other mother were born alive and survived.

There were 4 cases of placenta previa among the twin pregnancies and in 3 both twins died. All 6 twins weighed less than 1,500 Gm. The incidence of placenta previa does not vary appreciably from that found in association with single pregnancies. Davis[12] states that the total incidence in the Chicago Lying-in Hospital since the opening of the present building in 1931 is 1:102 or practically one per cent. The incidence of 1:83 among twins is probably accidental due to the smaller number of cases. Due to the greater proportionate part of the uterus occupied by the placenta in twin pregnancies one would expect that at least a marginal insertion might be somewhat more frequent.

There were 7 cases (2.1 per cent) of polyhydramnios in the series, one case being included under the pre-eclamptic group, and one under the hypertensive group. The incidence is lower than generally reported. The various estimates of polyhydramnios range from 3.6 per cent (McClure[11]) to 24 per cent (McIlroy[13]). Among the deaths in which polyhydramnios was the only complication both twins were previable in one case, a third was macerated, and the fourth died of intracranial hemorrhage.

Although the incidence of complications is somewhat higher in twin than in single pregnancies, maternal abnormalities do not in general seem to be responsible for the higher fetal and infant death rates. It is of particular interest that premature detachment of the placenta did not occur in twin pregnancies.

There were no maternal deaths in this series. In a group of 1,163 cases of viable twin pregancies collected from the recent literature by Guttmacher,[10] there were 23 maternal deaths (2 per cent). Adding our 305 cases of viable twin pregnancies to his series, there would be a combined maternal mortality of 1.5 per cent.

SUMMARY

Three hundred and thirty-four multiple pregnancies occurred in 31,131 total deliveries, an incidence of one in 93.4 for twins, and one in 15,514 for triplets.

The average birth weight is 2,391 Gm. for an infant which is one of twins and 3,405 Gm. for other infants born in this hospital.

The average length of gestation is 256 days in twin pregnancies, 281 days in all other pregnancies in this hospital.

The combined fetal and neonatal death rate for 660 reportable twin infants is 13.3 per cent; for twin infants over 1,000 Gm. it is 8.4 per cent. The total hospital mortality for reportable births is 4.4 per cent.

The incidence of hypertensive, pre-eclamptic and eclamptic toxemia among twins is more than three times that found in single pregnancies.

Prematurity is the outstanding cause of death in twin infants. Maternal complications are probably not an important factor in producing fetal death.

In this series the second born twin does not appear to have an increased birth hazard.

REFERENCES

(1) United States Department of Commerce. Birth, Stillbirth and Infant Mortality Statistics 1938, United States Printing Office. (2) *Potter, E. L., and Adair, F. L.:* J. A. M. A. **112:** 1549, 1939. (3) *Potter, E. L.:* Arch. Path. **25:** 607, 1938. (4) *Potter, E. L., and Adair, F. L.:* Fetal and Neonatal Death, 1940, University of Chicago Press. (5) *Daiser, K. W.:* Arch. f. Gynäk. **169:** 754, 1939. (6) *Adair, F. L., and Thelander, H.:* AM. J. OBST. & GYNEC. **10:** 172, 1925. (7) *Adair, Fred L.:* AM. J. OBST. & GYNEC. **20:** 539, 1930. (8) *Guttmacher, A. F.:* Ibid. **38:** 277, 1939. (9) *Goecke:* Arch. f. Gynäk. **169:** 317, 1939. (10) *Dieckmann, W. J., and Brown, I.:* AM. J. OBST. & GYNEC. **38:** 214, 1939. (11) *McClure, H. I.:* Ulster M. J. **6:** 284, 1937. (12) *Davis, M. Edward:* Unpublished data. (13) *McIlroy, A. L., and Evans, E. C.:* Med. J. & Record **126:** 359, 1927.

A CLINICOPATHOLOGIC STUDY FROM THIRTY-TWO CASES OF CHORIOEPITHELIOMA

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CHORIOEPITHELIOMA is such a malignant tumor, predisposed to early metastasis, and occurring not infrequently among women of childbearing age, that any data concerning it should be utilized with the view of its early recognition and consequent eradication. Hence the purpose of the present study.

This study, based on 32 cases, includes the patients that had been admitted in the obstetric, gynecologic and medical wards from February, 1937, to November, 1940. The fact that 32 cases of chorioepithelioma whose diagnosis has been established or corroborated by operation, histologic examination, x-ray, or autopsy findings occurred in the short span of three years and nine months, shows that the tumor is indeed far from being rare, at least in the Philippine General Hospital. Perhaps the earlier belief in the rarity of this tumor is not based on reality but on the failure of its recognition.

Incidence.—Among the 21,765 obstetric cases admitted from February, 1937, to November, 1940, 32 were cases of chorioepithelioma giving a proportion of 1 case of chorioepithelioma for every 680 obstetric patients. During the same period,

the relative incidence of chorioepithelioma among the different terminations of pregnancy was as follows:

1 chorioepithelioma for every 9.14 cases of mole
1 chorioepithelioma for every 474.44 cases of abortion
1 chorioepithelioma for every 4,563 cases of labor

The age incidence of chorioepithelioma among this set of cases was between 18 and 49. In a previous study, however, the youngest patient affected was 17 years.

We found that the chorioepithelioma is by far more common in multiparas than in primiparas. Of the 32 cases studied, 21 followed hydatidiform mole, 7 cases after abortion, and 4 cases after full-term labor.

In 3 of the 21 cases following mole, the mole and the chorioepithelioma were coexistent. One of these three was a case of twins where one was a live eight months' fetus with a normal placenta, and the other, a mole with metastatic chorioepithelioma in the vagina, lungs, and brain.

The fact that a normal placenta with its normal fetus may coexist with chorioepithelioma does not support Fleischmann's etiologic theory of chorioepithelioma which is the lack of a lytic substance in the maternal blood which normally prevents the abnormal invasion and proliferation of chorionic cells. For, if the theory were correct, then the coexistence of a normal placenta and chorioepithelioma would not be possible. The evidence seems to point out that the abnormality resides in the chorionic cell itself rather than in the maternal blood.

Of the 32 cases studied, 26 gave a history of uterine bleeding. The remaining 6 gave, respectively, the following complaints: pernicious vomiting, hypogastric pain and abdominal enlargement, headache and numbness of the left half of the body, unconsciousness and headache, vomiting and unconsciousness. In one case the symptoms indicative of brain metastasis occurred three years after an abortion. Twelve of the 32 cases had complications as follows:

Perforation of the uterus by the tumor	8 cases
Intestinal obstruction caused by the growth	1 case
Pneumonia	2 cases
Pulmonary tuberculosis	1 case

Of the 8 cases of uterine perforation, 2 had intra-abdominal hemorrhage, and 2 had pelvic abscess.

Twenty-one of the 32 cases showed metastasis in different organs at the same time as revealed by laparotomy and x-ray of the lungs or by autopsy. The relative frequency of the organs affected was as follows:

Lungs	18 cases
Vagina	5 cases
Brain	4 cases
Broad ligament	4 cases
Intestines	3 cases
Spleen	2 cases
Kidney	2 cases
Liver	1 case

Diagnosis.—In 25 of the 32 cases, there were three factors which were consistently found and which we have come to believe, when present, constitute a positive clinical method of diagnosis. These data are: (1) History of having passed mole or of having aborted; (2) uterine bleeding; and (3) the finding on abdominopelvic examination of an enlarged soft uterus as if it were pregnant. For easier remembrance, we have labeled these data as *H. B. Es.* in which *H* stands for history of a last pregnancy ending in mole expulsion, or abortion or even full-term delivery; *B* stands for uterine bleeding; and *Es* stands for the enlargement and softening of the uterus.

The uterine bleeding, which varied from slight to profuse, and was either continuous or intermittent, appeared any time within six months after the termination of

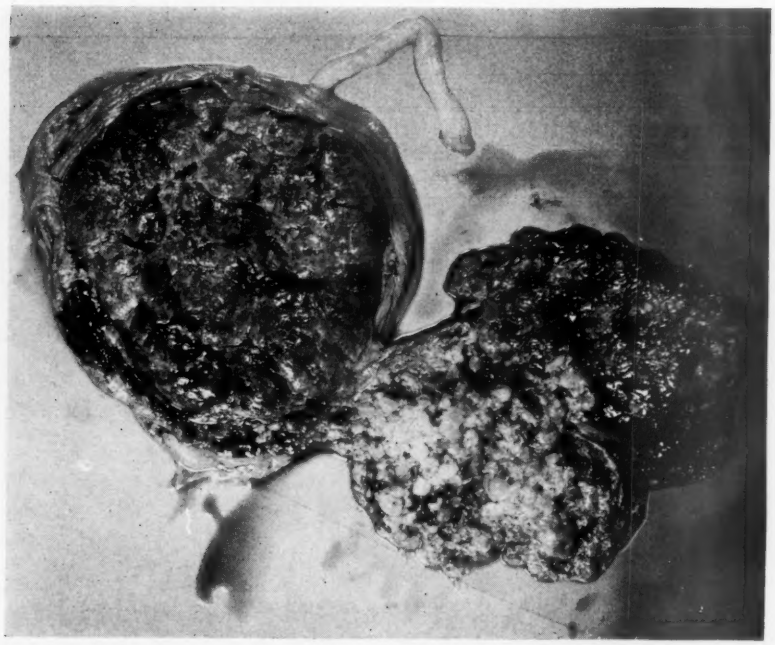

Fig. 1.—Normal placenta, mole, and chorioepithelioma. Twin pregnancy with one live eight months' fetus and a mole, which developed chorioepithelioma with metastases in vagina, lungs, and brain.

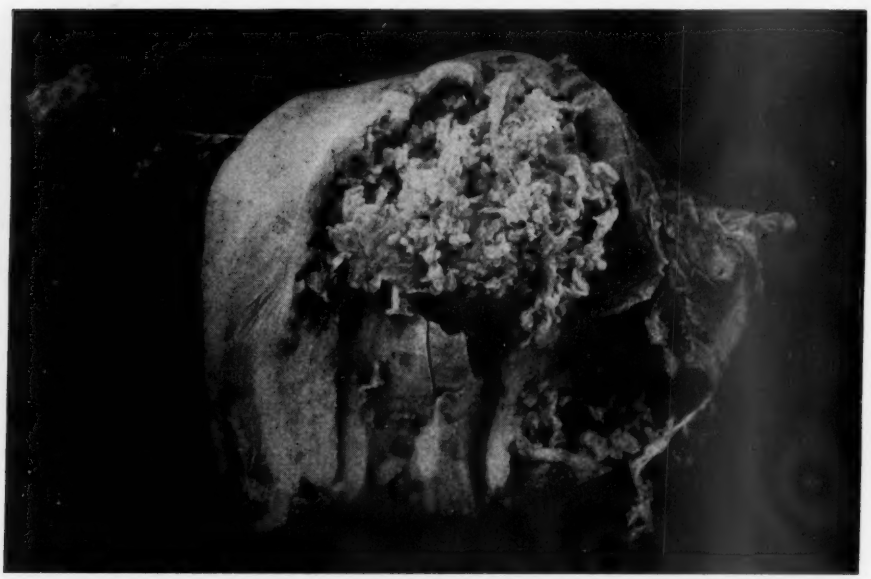

Fig. 2.—Chorioepithelioma of the uterus with metastasis into the right broad ligament.

the last pregnancy. The uterine bleeding should not be preceded by amenorrhea which may indicate pregnancy. The size and contour of the uterus depended on the size of the growth within and on the presence or absence of extension of the tumor in the surrounding vicinity of the uterus. In one case where the chorioepithelioma was of the size of a button 1.5 cm. in diameter, the uterus had the size of a one month's pregnancy. In another case, the size of the uterus was that of a four and one-half months' pregnancy.

The uterus affected with chorioepithelioma is soft when relaxed, but sometimes it contracts; then it becomes as hard as any contracting pregnant uterus.

An intelligent interpretation of the data as represented by *H. B. Es.* will rule out extrauterine pregnancy. Either case, however, calls for laparotomy. Uterine pregnancy with symptoms of threatened abortion should be eliminated.

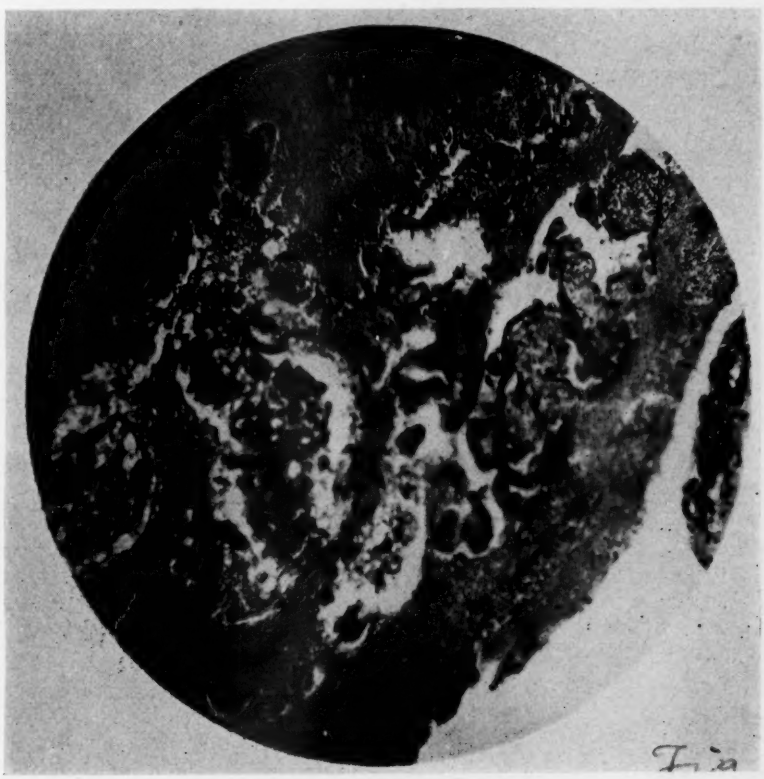

Fig. 3.—Microscopic section of the tumor of Fig. 2.

The senior author of this paper has done 13 hysterectomies on the basis only of the data represented by *H. B. Es.*, very often on the hour of admission to the hospital, and it was found that the positive diagnosis of chorioepithelioma in these cases was invariably supported by the gross and histologic examinations of the tumor in the uterus. Except in very doubtful cases where the uterus is not appreciably enlarged, we not only do not employ but also strongly object to the performance of the so-called "diagnostic curettage," a measure which most authors, if not all, believe to be the only way of making a positive diagnosis. We make diagnostic curettage only when the uterus is not enlarged and the diagnosis is doubtful. And we follow the verdict of the Friedman test only in doubtful cases when all the data as represented by *H. B. Es.* are not present.

The reasons for objecting to the performance of the diagnostic curettage in the presence of the data *H. B. Es.* are as follow:

1. If the result is positive, it merely confirms the diagnosis already made by the data *H. B. Es.*, and nothing has been gained.

2. If the result is negative, it will not alter the positive diagnosis arrived at through the data *H. B. Es.* nor the decision for radical treatment. In many of our cases, the tumor was found to be in the muscular wall far beyond the reach of the curette so that in these cases, uterine scrapings would have invariably given a negative finding.

Fig. 4.—Microscopic section of a perforated chorioepithelioma. Both Langhans' cells and syncytial cells are seen, with a preponderance of the former.

3. The use of the curette may give rise to infection in a uterus that, because of its softness, has become susceptible to germ growth.

4. The curette may perforate the uterus in cases where the growth has extended throughout the thickness of the uterine wall and thus increase the danger of a radical operation.

5. It may incite the rapid flaring up of metastasis.

6. At best, it is a misuse of time and energy unnecessarily, if not dangerously, delaying the performance of a radical operation which should be done as early as possible.

Friedman Test.—We follow the verdict of the Friedman test in cases where the data of the *H. B. Es.* are not present, also in the follow-up of cases after treatment.

Treatment.—Four patients with uterine chorioepithelioma were treated by x-ray. Only one patient was saved, and this was a very early case. The rest died. Nineteen cases were subjected to radical operation of hysterectomy in addition to salpingectomy, oophorectomy, and partial excision of the broad ligament in cases where these structures were affected by metastasis. Of these 19 cases, 6 had lung metastasis which was untreated by x-ray. These 6 patients died later from the extension of the lung metastasis. The death of these patients shows that the removal of the primary tumor does not bring about the recession of metastatic growth in other organs, as has been affirmed in obstetric literature.

One case of early lung metastasis was treated by x-ray. And this is the only case of lung metastasis in our series that recovered. This particular case was one wherein the chorioepithelioma had perforated the uterus with about 200 c.c. of blood in the peritoneal cavity and a thin metastatic growth over the rectum. The intestinal metastasis was treated by x-ray. It is now seven months since the operation and x-ray treatment, and the patient continues to be well, with a negative Friedman test.

Three of the patients with uterine chorioepithelioma had vaginal metastasis. These were treated by surgical enucleation of the vaginal tumor in addition to hysterectomy. One of the patients operated upon died of peritonitis due to the perforation of the uterus by the chorioepithelioma.

Of the 19 patients operated upon, 12 recovered.

One patient (the case cited above) was subjected to intramuscular injection of serum from a pregnant woman for the purpose of giving her the benefit of the lytic substance postulated by Dickson, Mathieu, and others as existing among pregnant and puerperal women who do not develop chorioepithelioma. However, since this patient was also treated surgically and by x-ray, we cannot attribute her cure to the intramuscular injection of the puerperal blood serum.

The result of this study points to early hysterectomy and early x-ray exposures of the lung metastasis as the surest form of treatment. X-ray treatment for uterine chorioepithelioma may be considered only in very early cases and where a contraindication exists for laparotomy; and patients receiving such form of treatment should be carefully followed up for the return of the symptoms of bleeding or for the positive Friedman test. Moderately advanced cases do not yield to x-ray treatment.

SUMMARY AND CONCLUSIONS

1. This study is based upon 32 cases of chorioepithelioma.

2. Chorioepithelioma may occur in individuals from the age of 17 to 49 years.

3. Chorioepithelioma is more common in multigravidas than in primigravidas.

4. It may occur after full-term labor, but it is more common after abortion and especially after mole expulsion.

5. Symptoms indicative of chorioepithelioma may appear from the day after the termination of pregnancy to three years thereafter.

6. The belief that the chorionic cell is abnormal per se, and that in normal women it does not develop into chorioepithelioma because of the supposed presence of a lytic substance, is not supported by the co-

existence in a case of twins, of a normal placenta with its live fetus and a hydatidiform mole and metastatic chorioepithelioma.

7. The removal of the primary chorioepithelioma does not bring about the reabsorption of its metastasis.

8. A clinical method of diagnosis of chorioepithelioma is presented.

9. Friedman's test in chorioepithelioma is evaluated.

10. Negative x-ray findings in lungs for chorioepithelioma in the presence of lung symptoms do not necessarily indicate absence of metastasis unless proved otherwise or unless the negative findings persist four to five weeks after the first examination.

11. Surgical removal of the tumor in accessible places and early x-ray treatment of the lungs, should they be affected by metastasis, give the highest percentage of recovery.

We wish to acknowledge our indebtedness to Dr. Wilfrido de Leon who made the microscopic examinations of the specimens.

REFERENCES

(1) *Acosta-Sison, H., and Galang, J.:* J. Philippine M. A. **17:** 457, 1937. (2) *Fleischman:* From Mathieu and Robertson, Surg. Gynec. & Obst. **69:** 158, 1939. (3) *Dickson, J. C.:* U. S. Nav., M. Bull. **33:** 358, 1935. (4) *Mathieu, A., and Robertson, T. D.:* Surg. Gynec. & Obst. **69:** 158, 1939.

A COMPARATIVE STUDY OF PREGNANCY IN THE WHITE AND COLORED RACES*

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A COMPARATIVE study of pregnancy in a series of 1,000 indigent white women with 1,000 consecutive pregnancies in colored women, all residing in Mecklenburg County, North Carolina, is here presented. By way of introduction, the notoriously high maternal death rate in the southern United States has primarily been ascribed to social and economic causes, a major factor being the large percentage of the childbearing populace that are members of the colored race. The maternal mortality rate among negroes throughout the country has always been higher than among whites and has failed to show the substantial reduction that has applied in the white mortality during the past few years. In the United States the rate for negroes in 1938 was 8.6 per 1,000 births as compared with 9.3 in 1934, a reduction of 8 per cent. The mortality rate for white mothers in 1938 was 3.8 per 1,000 births as compared with 5.4 in 1934, a reduction of 30 per cent. In other words the maternal mortality rate among negroes throughout the entire United States in 1938 was more than double the white mortality rate. North Carolina was quite comparable with the United States as a whole in this respect, the

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total maternity death rate in 1938 being 5.6 per 1,000 live births, divided as follows: white, 4.4; negro, 8.3.

The comparative study of 2,000 consecutive pregnancies here presented was undertaken as an effort to ascertain if the colored patient is a greater obstetric hazard than the white patient living under similar social and economic circumstances. The private white patient naturally utterly fails as fair comparative data. The 1,000 consecutive white pregnant women herein reported were all indigent patients living in the poorer sections of the city or on tenant farms, and their dietary, economic, and environmental circumstances are comparable to the negro. Such comparisons as are here presented, expanded on a wide scale might

TABLE I. COMPARATIVE MORTALITY RATE BY RACE, FROM THE NORTH CAROLINA BUREAU OF VITAL STATISTICS

	WHITE	COLORED
1930	6.7/1,000	12.2/1,000
1932	5.8	10.3
1934	6.7	9.7
1936	5.9	9.6
1938	4.5	8.4
1939	4.0	6.7
Total deaths 1930—640		
Total deaths 1939—394		

TABLE II. INCIDENCE OF PRENATAL CARE

	1,000 COLORED	1,000 WHITE
None	2.1%	10.8%
Inadequate (4 visits or less)	29.0%	33.0%
Good	68.9%	56.2%

Comment.—The Charlotte Maternity Clinic offers a prenatal service for indigent patients by means of a large central city clinic and five subclinics in rural sections of the county. This means that prenatal care is readily accessible to every resident of the city and county. In the early years of this program, it was thought that the negroes would be too indifferent and ignorant to avail themselves of this service. Such has not been the case; rather the white patient has proved to be less responsive and more immune to maternal welfare education than the negro. One hundred and eight white patients in this series had no prenatal care as compared to only 21 negroes. Six hundred and eighty-nine negroes had excellent prenatal care as compared to 562 whites. The illiterate white class is in many respects a greater social problem than the negro. Apparently they are less receptive to organized and competent maternal care.

TABLE III. AGE GROUP

	1,000 COLORED	1,000 WHITE
10-19 years	35.2%	20.5%
20-29 years	50.0%	51.0%
30-39 years	14.0%	25.0%
40 plus years	0.8%	4.5%

Comment.—This analysis conforms with the accepted knowledge as to the early reproductivity of the negro and likewise her declining fertility in the fourth and fifth decades of life.

aid in answering some of the problems of the high maternal mortality in the southern states. Is the southern rate high because of the negro or is it because of the social and economic circumstances under which she lives and breeds. In short, is race per se really a factor in maternal mortality? (Table I.)

TABLE IV. GRAVIDITY

	1,000 COLORED	1,000 WHITE
Primipara	30%	22%
Multipara	70%	78%

TABLE V. HEMORRHAGE

	1,000 COLORED	1,000 WHITE
Post partum	2.1%	2.3%
Placenta previa	0.5%	0.3%
Premature separation of placenta	0.5%	0.6%
Total	3.1%	3.2%

Comment.—No racial difference is noted in the study of hemorrhages complicating pregnancy.

TABLE VI. LABOR

	1,000 COLORED	1,000 WHITE
Precipitate delivery	27.9%	14.2%
Labor over 24 hours	6.4%	6.6%
Labor over 48 hours	1.1%	1.5%

Comment.—Aside from a higher incidence of precipitate delivery in the negro (naturally high in any home delivery service), there is no striking racial difference in the duration of labor. The incidence of prolonged labor is quite similar in the two races.

TABLE VII. OPERATIVE INCIDENCE

	1,000 COLORED	1,000 WHITE
Low forceps	1.2%	3.7%
Midforceps	0.4%	0.7%
Version	0.4%	0.1%
Breech extraction	0.2%	0.6%
Curettage	0.0%	0.2%
Hysterotomy	0.6%	0.3%
Cesarean section	0.9%	1.0%
Total	3.7%	6.6%

Comment.—The operative incidence in the white race of 6.6 per cent is higher than the incidence in the negro of 3.7 per cent, chiefly because of a greater use of low forceps in the white patients (37 cases in the white as compared to 12 in the 1,000 negroes). Elimination of this variation leaves a similar incidence of major obstetric procedures in the two races. Even the operation of cesarean section shows no racial difference: 9 cases in 1,000 whites and 10 cases in 1,000 negroes.

From the study of duration of labor and operative incidence, no clinical pelvic racial variation occurs that is not well compensated for by other factors. The end result of delivery confirms this observation. While a contracted pelvis is generally accepted as more frequent in the colored race, nature apparently produces a termination of pregnancy that is as effective as in the white patient.

Even in a fairly concentrated area of population where adequate maternal and hospitalization facilities are provided, the ignorance and low mentality of the indigent patient frequently result in a failure to

TABLE VIII. TOXEMIA OF PREGNANCY

	1,000 COLORED	1,000 WHITE
Pre-eclampsia	11.40	6.90
Eclampsia	1.5	0.5
Hypertensive vascular disease	5.8	7.9
Total	18.7%	15.3%

Comment.—The incidence of eclamptogenic toxemia of pregnancy appears higher in the negro than in the white cases studied. This is the most positive finding in this study and might be interpreted as a contributing cause of the higher negro maternal mortality reported in vital statistics.

TABLE IX. INDUCTION OF LABOR

	1,000 COLORED	1,000 WHITE
Bag	0	0
Rupture of membranes	1.7%	2.8%
Bougie	0.1%	0.1%

TABLE X. COMPLICATIONS

	1,000 COLORED	1,000 WHITE
Organic heart disease	0.6%	0.6%
Tuberculosis	0.5%	0.3%
Fetal abnormalities	0.5%	1.4%
Syphilis	23.7%	5.9%
Puerperal infection	0.8%	1.9%

Comment.—The high incidence of syphilis in the colored patients (237 cases in this series of 1,000 deliveries) while probably not a factor in maternal mortality requires comment as a contributing cause of maternal morbidity and fetal mortality. Likewise the higher incidence of fetal abnormalities in the white patients (1.4 per cent white, 0.5 per cent colored) is in conformity with published observations on this subject.

No other striking differences in the incidence of medical complications were noted.

An apparently higher incidence of infection in the white patients is not worthy of evaluation, as the delivery of the majority of these patients in the home did not permit an accurate study of morbidity.

TABLE XI. INFANT MORTALITY

	1,000 COLORED	1,000 WHITE
Miscarriage	2.4%	3.4%
Stillbirths	4.0%	3.3%
Neonatal deaths	4.2%	3.0%
Total infant loss	10.6%	9.7%

Comment.—No striking racial difference appears in the incidence of stillbirths. The incidence of miscarriage is near similar. The higher incidence of neonatal deaths in the colored (4.2 per cent) as compared to the white (3.0 per cent) is probably related to the higher incidence of syphilis in the former.

TABLE XII. MATERNAL MORTALITY

	1,000 COLORED	1,000 WHITE
Premature separation of placenta	0	1
Pneumonia	0	1
Post-partum hemorrhage	1	1
Ruptured uterus	1	0
Spinal anesthesia	1	0
Eclampsia	1	1
Acute pre-eclampsia	0	1
Chr. hypertensive disease	1	0
Post-partum infection and toxemia	0	1
Total	5	6

Comment.—Toxemia of pregnancy was a major factor in 5 of the 6 white maternal deaths and in 3 of the 5 colored maternal deaths.

TABLE XIII. ASSIGNMENT OF MAJOR RESPONSIBILITY FOR MATERNAL DEATHS

	COLORED	WHITE
Unavoidable	0	2
Physician	2	2
Patient	3	2

Comment.—From the standpoint of assignment of primary responsibility the maternal deaths occurring in this series of 2,000 indigent patients may be divided into three arbitrary groups: those due to the patient, those due to the physician, and those nonpreventable.

utilize such services. Often a failure at intelligent cooperation, a condition not unusual in this class of individual, directly results in a maternal death.

In discussing maternal deaths due to errors in medical judgment, the very nature of a free clinic service presents limitation of professional interest and a lower professional standard than that represented in the relationship of qualified private physicians to paying patients. In addition to inadequate medical supervision, the problem of a changing and inexperienced medical personnel, the inevitable price of a teaching service, can unfortunately be involved as a factor in maternal mortality.

Third and last are the group of nonpreventable maternal deaths. The irreducible minimum has yet to be defined but the nature of pregnancy itself results in hazards in any race that are occasionally fatal.

CONCLUSIONS

1. The incidence of toxemia of pregnancy and of syphilis is higher in the colored than in the white race.

2. No striking racial differences were noted in the incidence of hemorrhage, infections, operative deliveries or other contributory causes of infant and maternal mortality.

3. Toxemia and chronic vascular pathology, together constitute the outstanding pathologic factor in maternal mortality occurring in the indigent, being the major or contributing cause in the death of 8 of the 11 maternal deaths in this series of 2,000 patients.

4. The negro patient is often more appreciative, cooperative, and receptive to an organized maternal welfare program than the indigent southern white.

5. The high maternal mortality throughout the southern United States is not primarily due to the colored race but due to the social and economic circumstances confronting a large percentage of the populace, including the negro. Race per se is not a major contributing factor in maternal mortality.

Indebtedness and appreciation are hereby expressed to Dr. Everett Sawyer for his aid in collecting data summarized in this paper.

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PLASMA IN OBSTETRICS*

With a Simple Method for Its Production

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THE efficacy of plasma in the treatment of hemorrhage and shock, whatever its nature, is now well known.[1, 2] Plasma is peculiarly adapted for obstetric needs. Obstetric hemorrhage and shock require immediate and adequate replacement of blood volume. Until recently, this meant transfusion of whole blood procured either from actual donors or from a blood bank. In the case of donors, actual time trials have shown that an average of at least two hours will elapse from the time donors are called until blood is available. Even if the donor is present in the hospital, necessary preparations require forty-five minutes before transfusion may be given. In the case of blood banks further time trials have shown that a minimum of thirty minutes is required before blood is available. Furthermore, blood banks are not unfailing sources of supply. Even the largest bank may find it impossible to supply a call for one of the rarer blood types or be unable to furnish blood in the quantity needed. On the other hand, plasma is immediately available. There is no need for typing or crossmatching. Plasma may be pouring into the patient's veins one minute after the need becomes apparent.

Convinced that plasma should play a prominent role in the control of the important maternal mortality hemorrhage factor, a plasma bank was organized in November, 1940, in the Department of Obstetrics and Gynecology of St. Catherine's Hospital under the direction of Dr. Charles A. Gordon. The experience of the Blood Transfusion Association of New York[3] in collecting blood for plasma had shown that the closed vacuum system of collecting blood and drawing plasma was an ideal method, because of ease of technique and preservation of sterility. The results of our use of plasma in the treatment of obstetric hemorrhage and shock have been so striking that we now feel that no lying-in institution is properly equipped unless plasma is available for immediate

*Read, in part, at a meeting of the Obstetric Conference of the Committee on Maternal Welfare of the Medical Society for the County of Kings, March 25, 1941.

use. A simple, cheap and practical method for the production and administration of plasma has been developed. It may be easily installed in any hospital, however small.

The equipment necessary for the production of plasma follows:

1. A donor valve set.
2. A vacuum bottle containing 70 c.c. of 2½ per cent sodium citrate in physiologic saline.
3. A vacuum bottle containing 250 c.c. of physiologic saline.
4. An aspirating needle.
5. An icebox.
6. A record system.

The problem of procuring donors was readily solved. It is routine, on the admission of any patient with a history of bleeding, to send for donors who are promptly typed and crossmatched, in order to be prepared for transfusion, if it should become necessary. Now, instead of typing prospective donors until one with a suitable cross match is found, blood for the plasma bank is drawn from each one of them. They are told that if their blood is not used for their relative or friend, it will be used for some other patient in need of a transfusion. Another small but valuable source of plasma is phlebotomy. When a plasma bank is established it becomes self-supporting, as recipients of plasma are told that a relative or friend must donate blood to make up for what has been given to them. We have not as yet failed of repayment. In fact, we often obtain a double return.

PROCEDURE FOR PRODUCTION OF PLASMA

A complete physical examination is performed on the donor who signs an agreement to donate his blood to the plasma bank. Under operating room aseptic technique, slightly over 500 c.c. of blood is drawn, using the donor valve set, into a vacuum bottle containing 70 c.c. of 2½ per cent sodium citrate in physiologic saline solution. The blood remaining in the tubing is drained into a test tube, which is sent to the laboratory for typing and serology. The typing of the blood is unnecessary, but is done for our own studies and for the donor's information. The citrated blood is then placed in the icebox at 4° C.

The blood is kept in the icebox for from five to seven days. It has been shown that sedimentation of the cells is greatest at this time, while hemolysis is minimal. The citrated blood has now separated into two layers. The lower layer is composed of cells; the supernatant fluid is the plasma which may now be drawn off. A greater yield of plasma may be obtained by centrifugation, but this entails the addition of costly apparatus and a considerable increase in the detail of technical procedure. Furthermore the difference in the yield of plasma by centrifugation and sedimentation is but 30 to 50 c.c. Largely because we wished to establish a simple as well as an inexpensive technique, sedimentation appeared to be a satisfactory way to obtain plasma. This we have found to be so.

The aspiration of plasma is also done under aseptic technique. By means of the same donor valve set used in drawing blood, the supernatant plasma is aspirated into a vacuum bottle containing 250 c.c. of physiologic saline solution, substituting a long aspiration needle for the venipuncture needle (Fig. 1). While undiluted plasma may be

used, the addition of saline solution inhibits precipitation of fibrin, which is more likely to occur in the undiluted plasma. Scrupulous care must be taken not to aspirate any of the cells and, when near the bottom of the plasma layer, the rate of flow should be carefully controlled by the valve. This precaution necessitates leaving a small layer of plasma, usually about three-sixteenths of an inch in depth. Nevertheless, the average yield of plasma from 520 c.c. of citrated blood is abut 250 c.c. When the aspiration is completed, the plasma remaining in the tubing is collected and cultured. No antiseptic is used, though many have advised the addition of 5 c.c. of 1 per cent merthiolate solution. We feel that this added step in the procedure, because of the closed system and aseptic technique, is unnecessary. All our cultures have remained sterile.

It should be said that we have not found it necessary to pool plasma. Pooling is done to avoid a high agglutinin titer. However, there is considerable evidence to show that the presence of a high agglutinin titer is harmless.[4] Since this procedure entails added steps in the production

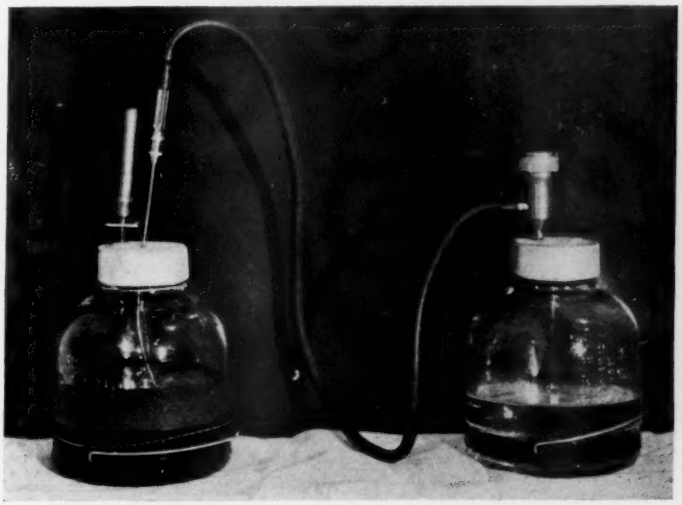

Fig. 1.—Aspiration of plasma.

of plasma, with a greater likelihood of contamination, we have omitted it from our technique. We have given close to 100 plasma transfusions and have had no reactions, though we have made no effort to give plasma of the same type as the recipient.

Plasma is ready for use as soon as the culture is reported negative. No special facilities are required for its storage. It may be kept in a closet, on a shelf, utility room, or any available place. It need not be stored in an icebox. As far as is known, plasma may be safely used after long periods of time.

Plasma is administered in exactly the same manner as a venoclysis, with the exception that the plasma is passed through a steel mesh filter to keep out any precipitate that may have formed (Fig. 2). Sterile recipient sets which contain the tubing, needles, and steel filter necessary for the administration of plasma are kept available in the delivery room. The patient in shock may be receiving plasma one minute after the order is given for its use.

CASE REPORT

CASE 1.—A. M., aged 28 years, para 0, gravida i, expected date of confinement June 9, had a normal antenatal course. She entered the hospital May 31 in active labor. Following a twelve-hour labor, the patient was delivered by low forceps under gas oxygen ether anesthesia of a 6-pound 8-ounce living female in good condition. Placenta was delivered intact ten minutes later; blood loss was 200 c.c. One and one-half hours following delivery, patient suddenly had a profuse hemorrhage of 750 c.c. and went into profound shock. The uterus was massaged manually and ergotrate administered intravenously. Five hundred cubic centimeters of 50 per cent plasma in saline were given immediately. After twenty minutes the condition of the patient was improved and one hour later, another 500 c.c. of plasma solution were given. Patient's condition became normal and signs of shock disappeared. Post-partum course was uneventful thereafter, except for an anemia, for which she received a transfusion of 500 c.c. of citrated blood on the third post-partum day.

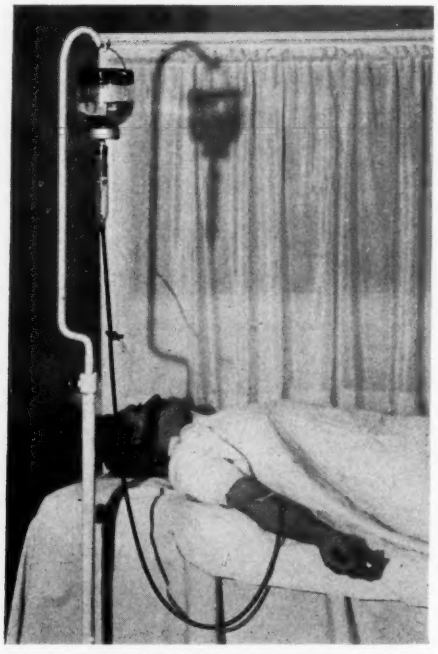

Fig. 2.—Administration of plasma through steel mesh filter.

CASE 2.—A. S., aged 26 years, para 0, gravida i, expected date of confinement March 7, had a normal antenatal course, and entered the hospital March 14 in active labor. Examination disclosed a frank breech presentation in the L.S.P. position. Pains were desultory and progress slow. The fetal heart disappeared after twenty-six hours of labor. After fifty-four hours of labor, the cervix was fully dilated, a Bandl's contraction ring was present and the mother was in poor condition. Under gas oxygen either anesthesia, the anterior leg was delivered by fracturing the femur. The posterior leg was delivered by means of a Braun's hook. Because of the contraction ring, the head could only be delivered by means of a cephalotribe. Following delivery, the patient was in deep shock. Five hundred cubic centimeters of 50 per cent plasma in saline were given with immediate improvement. The post-partum course was uneventful, except for a slight rise in temperature the first three days.

CASE 3.—R. P., aged 25 years, para 0, gravida i, expected date of confinement April 13, had a normal antenatal course, and was admitted to the hospital April

17 in active labor. Following a thirty-hour labor, patient delivered spontaneously a living female child, weighing 5½ pounds. One half hour after delivery with the placenta still undelivered, patient lost about 600 c.c. of blood and went into deep shock. Five hundred cubic centimeters of 50 per cent plasma in saline were given immediately, followed by another 500 c.c. of plasma solution, with marked improvement in the patient. Patient was then given a general anesthesia and the placenta removed manually with ease. There was no further bleeding following this. Subsequent post-partum course was uneventful.

CASE 4.—M. S., aged 34 years, para 0, gravida i, expected date of confinement December 21, was admitted to the hospital January 3, because of a pre-eclamptic toxemia. Patient was placed on routine toxemia therapy, and three days after admission went into labor. After a twelve-hour labor, cervix was fully dilated, and the head was on the perineum. Blood pressure at this time was 168/100. Patient was placed on the delivery table, following which, she had a convulsive seizure lasting three minutes. Low forceps were immediately applied without anesthesia and a living female child weighing 7½ pounds was delivered from the L.O.A. position. The placenta delivered twelve minutes later. Immediately thereafter patient had another convulsion lasting three minutes, followed by a profuse hemorrhage of 1,500 c.c. with resultant profound shock. Plasma therapy was quickly instituted and 1,000 c.c. administered. There was an immediate and marked improvement in the patient's condition. Post-partum course was subsequently normal except for an anemia, for which transfusions of 500 c.c. of citrated blood were given on the second and seventh post-partum days. There were no further convulsions and the blood pressure on her discharge, twelve days post partum, was normal.

CASE 5.—M. M., aged 34 years, para iii, gravida iv, was admitted February 9 with a history of the last menstrual period being December 7, and of profuse vaginal bleeding accompanied by abdominal cramps for the past twenty-four hours. Patient was admitted in deep shock. Two thousand cubic centimeters of 50 per cent plasma in saline were given in the course of three hours with marked improvement in the patient. Patient was taken to the operating room and under gas oxygen ether anesthesia, a large piece of placental tissue was removed. Postoperative course was uneventful and the patient discharged on the seventh postoperative day.

CASE 6.—M. R., aged 29 years, para i, gravida ii, expected date of confinement February 14, was admitted January 23, for an elective cesarean section. She had a cesarean section performed in 1938 because of a deformed pelvis, secondary to an attack of acute anterior poliomyelitis. On January 28, an elective two flap lower segment cesarean section with transverse incision was performed under local infiltration of 1 per cent procaine. Following delivery of the baby, patient lost about 600 c.c. of blood and evidenced signs of shock. One thousand cubic centimeters of plasma solution were immediately given and patient's condition became markedly improved. Postoperative course was normal except for an anemia for which she received a transfusion of 500 c.c. of citrated blood on the third post-partum day. She was discharged on the fifteenth post-partum day.

As stated above, we have seen no reaction follow the use of plasma. This coincides with the greater experience of Elliot[2] and Strumia.[1] Any reaction to plasma that has been reported may be traced to pyrogens. Scrupulous and painstaking washing of tubing, donor valve and filter is of the utmost importance. A detailed technique for this procedure has been satisfactorily worked out.

The actual cost of setting up the plasma bank, including the cost of all the apparatus needed, exclusive of the icebox, was less than twenty-five dollars. The actual cost of producing 500 c.c. of 50 per cent plasma in saline solution is less than two dollars.

CONCLUSIONS

1. Plasma is an important addition to our obstetric armamentarium.

2. Plasma may be easily and cheaply obtained.

3. Because of its easy production and low cost, no hospital should be willing to accept obstetric patients unless plasma is available.

I wish to acknowledge the interest and help of Dr. Charles A. Gordon in the preparation of this manuscript.

REFERENCES

(1) *Strumia, M. M., Wagner, J. A., and Monaghaghn, J. F.:* J. A. M. A. **114:** 1137, 1940. (2) *Elliot, J., Tatum, W. L., and Busby, G. F.:* Military Surgeon **88:** 118, 1941. (3) Report of the Blood Transfusion Association, New York, 1941, Blood Transfusion Association. (4) *Elliot, J.:* Quoted from the Report of the Blood Transfusion Association, p. 82, January, 1941.

868 PROSPECT PLACE

ADENOMYOSIS INTERNA UTERI AS A CAUSE OF UNCONTROLLABLE ATONY AND HEMORRHAGE FOLLOWING CESAREAN SECTION FOR SACCULATION PREGNANCY. HYSTERECTOMY*

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ADENOMYOSIS of the uterus is a well-recognized cause of pain and irregular bleeding, and is often associated with impaired fertility. In the event of pregnancy it may lead to abortion, premature labor, or dystocia. Its relation to post-partum atony and hemorrhage has received scant notice in the literature, except for certain accidents due to endometriosis of operative or cesarean scars. In a previously unoperated primigravida, adenomyosis leading to spontaneous rupture of the uterus at the onset of labor was reported in 1937 from the Bellevue service by Melvin Stone.[1] He referred to a similar case described by R. Richardson in 1919. Two others are collected by Batizfalvy;[2] and he cites a report in 1927 by Schweitzer,[3] who was forced to amputate the uterus for atony following cesarean section and found it honeycombed with endometriosis. Hysterectomy for atony and hemorrhage following *normal* delivery was performed by Szenes[4] who reported (1928) similar findings. The paucity of such reports may be due to the fact that pathologic study is available only in the rare cases coming to hysterectomy or to autopsy.

CASE REPORT

Mrs. M. A. (No. 62810) was first seen March 5, 1936, in the second month of her first pregnancy at 30 years of age. Four years previously she had undergone an appendectomy, resection of cystic left ovary, and round ligament suspension by the Coffey technique. It should be emphasized that ventral fixation was *not*

*Read at a meeting of the New York Obstetrical Society, May 13, 1941.

done. Menses began at 16, cycle was thirty to thirty-five days, duration and amount average, with mild suprapubic pain for one week before the periods. The general physical examination, blood pressure, and urinalyses were normal, and nothing unusual was noted about the pregnant uterus or cervix.

After a normal pregnancy, labor began spontaneously at forty weeks and remained very active throughout a trial of thirty hours. Examination under anesthesia revealed the cervix extremely high posterior, difficult to reach, very long and tough, and dilated 1.5 cm. The baby lay in R.O.P. with the unengaged head distending the anterior wall of the lower uterine segment far removed from the cervix. The pelvis was entirely ample and the diagonal conjugate was not reached at 13 cm. Under the diagnosis of anterior sacculation pregnancy,[5] cesarean section was performed because of the failure of a thirty-hour trial labor to produce cervical dilatation or engagement of the head.

A living 7 pound 13 ounce (3,544 Gm.) female infant, which survives, was delivered on Oct. 13, 1936, by low flap cesarean section. The skin incision avoided the previous laparotomy scar and care was taken not to disturb the plicated round ligaments, which were spread out over the anterior uterine wall producing several peritoneal folds. The Coffey suspension had *not* resulted in any adhesion to the parietes, the resected left ovary was so thinned out as to be unrecognizable, and the tube spread over the left uterine border. The right adnexa lay free in the lumbar gutter. The lower uterine segment was incised longitudinally and closed in layers with chromic catgut sutures. It is to be noted that the uterus behaved normally through labor and at cesarean, contracting well with the aid of pituitrin 0.5 c.c. intravenously after delivery of the baby, and one ampoule each of pituitrin and ernutin after removal of the secundines. The patient was afebrile on and after the fifth day and was discharged on the sixteenth day, when the cervix was still too high to palpate vaginally.

At follow-up examination one month post partum, the cervix had descended to normal position and the corpus was anterior and mobile. Menses now occurred at irregular thirty-five- to forty-two-day intervals, their prolonged duration and associated cramps being attributed to a stenosis of the upper cervical canal. Although contraceptives were employed only six months, another twelve months elapsed before conception occurred.

Examination in the eighth week of the second pregnancy revealed decreased uterine mobility, and a high posterior cervix with mild chronic inflammation. Pregnancy was again uneventful and elective cesarean section was done February 11, 1939, at forty weeks by the same method. An 8 pound 9 ounce (3,884 Gm..) female infant was delivered and now survives. This time the uterus looked healthy, and the round ligaments and adnexa as at the former cesarean; and the lower uterine segment was covered by numerous reduplications of peritoneum, permitting ample upper and lower flaps to be developed. The lower segment was again incised longitudinally, and after removal of infant and complete membranes and placenta it was again closed in layers with chromic catgut. The usual intravenous pituitrin after delivery of the baby and ergotrate after removal of the secundines were given and the initial blood loss was about average during the closure of uterus and peritoneal flaps. Before the abdominal closure was begun, however, the anesthetist reported a rapidly rising pulse rate and alarming drop in blood pressure. Direct examination revealed a very flabby uterus filling with blood, and reaching the diaphragm. Large amounts of blood were expressed; but despite intravenous ergotrate, massage and application of hot towels to the uterus, it failed to contract and the radial pulse became imperceptible.

Meanwhile an intravenous infusion of 10 per cent glucose in saline was started, and within a few minutes 700 c.c. of whole blood was transfused directly from the husband. Supravaginal hysterectomy with removal of the remnant of left adnexa was done and an attempt made to spare the right adnexa. Because of active bleeding in the mesosalpinx, the tube had to be secondarily removed but the right ovary was conserved. The operating time for the three procedures was two hours. A second blood transfusion of 500 c.c. was given after the patient was returned to her room. The wound again healed by primary union and the

secondary anemia was sufficiently improved to permit discharge on the twenty-fifth post-partum day. The patient remains in normal health up to the present time, except for a susceptibility to trichomonas vaginitis readily controlled by estrogenic therapy.

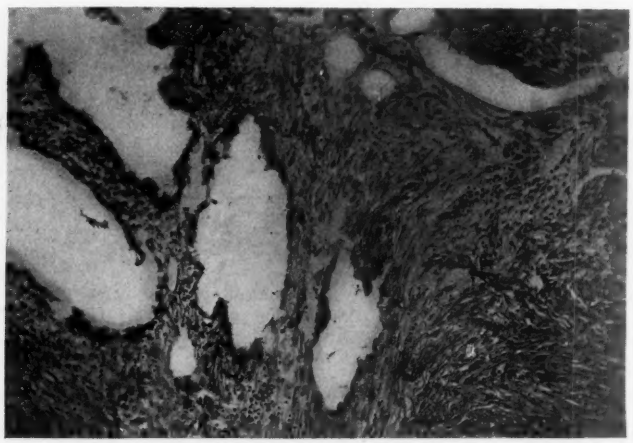

Fig. 1.—Adenomyosis interna uteri. Papillary and cystic hypertrophy of glandular elements of endometrioid islets in myometrium.

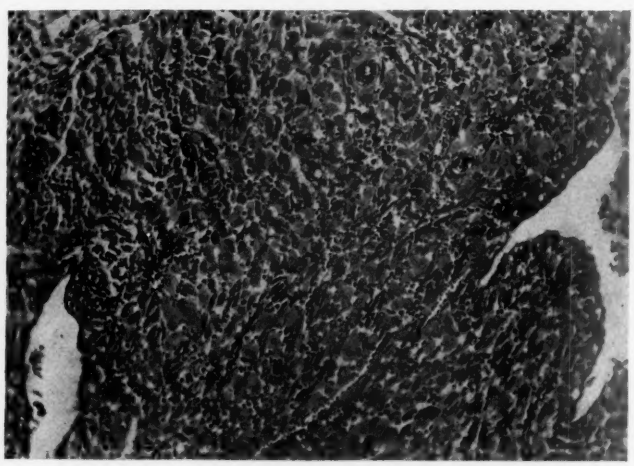

Fig. 2.—Adenomyosis interna uteri. Marked decidual reaction in stroma of endometrioid foci, causing dissociation of fibers of myometrium.

Pathologic Report by Dr. Motyloff.—Membranes, cord, and placenta were complete and grossly normal in both pregnancies. The hysterectomy specimen included congested edematous fragments of the tubes but no recognizable ovarian tissue. The uterus measured 18 by 16 by 12 cm., and a cuff of cervix 5 cm. wide and 2 cm. long was attached anteriorly. The anterior surface presented two pockets, on right and left sides, resulting from the Coffey operation. The freshly sutured cesarean incision ran from the amputated border 8 cm. upward parallel and slightly to the right of the midline. The uterus was opened through its posterior wall to permit inspection of this incision. The area near it was occupied by a scar, apparently the remnants of the previous section. The lining was rough, the actual site of the placenta could not be determined, and there was a small amount of clotted blood in the cavity.

The myometrium was pale, its cut surface looked like a sponge and presented a network of wide spaces which appeared empty on dissection. There was no interstitial hemorrhage.

Microscopically.—The remnants of decidua were scant or completely missing in most sections. The myometrium had the appearance typical of pregnancy. There was no evidence of inflammation nor of vascular wall changes. Sections through the old cesarean scar showed fibrosis *without any other pathologic change.*

The submucous layer of the myometrium contained many large foci of adenomyosis. The stroma of the endometrial islets showed marked decidual reaction, while the glandular elements were so extensively proliferated as to form small cysts. The foci were so numerous and so large as to cause dissociation of the muscle fibers in the myometrium (Figs. 1 and 2).

Diagnosis.—Puerperal uterus; adenomyosis interna uteri with pronounced decidual reaction; edema and congestion of tube.

DISCUSSION

In view of the normal uterine behavior at first cesarean section even after thirty hours of active labor, it was difficult to explain the profound atony, hemorrhage, and shock following the second cesarean. The latter was done by election, at term, under ideal conditions, and with no new technical difficulty. In both cases nitrous oxide and ether anesthesia by the closed method was well taken. The operative technique was the same except for time taken to excise the skin scar. Since the second baby was only 12 ounces (340 Gm.) heavier than the first, and since no labor was allowed, the sacculation of the uterine wall was probably no greater and possibly less than before. In standard textbooks sacculation[5] is reported as a cause of dystocia and uterine rupture but not post-partum atony.

Normal afebrile convalescence from the first cesarean section and the appearance of the uterus at the second operation both indicate that the intrinsic muscular, vascular, and nerve structure had been damaged little, if at all. The old scar showed no endometriosis or other demonstrable weakness.

There had been no intercurrent illness. But the menses had become more painful and prolonged, and the cycle varied from thirty-five to forty-two days. This, and the delay of conception for twelve months after the last use of contraceptives, could have been due to adenomyosis of the uterus.

The extensive invasion of the myometrium by endometriosis in the present case seems the most likely cause of the atony and hemorrhage. In the so-called Couvelaire uterus, dissociation of the muscle fibers by extravasated blood is believed to destroy their contractile power. Whether similar dissociation by endometrioid islets is extensive enough to cause post-partum atony and hemorrhage cannot yet be definitely stated. In four cases from the literature, it seemed the obvious cause of spontaneous uterine rupture, even in the first pregnancy in one of them. In Schweitzer's case as well as the present case, it seemed the most obvious cause of atony after cesarean section.

CONCLUSION

A case is presented of elective repeat cesarean section for sacculation pregnancy followed by uncontrollable uterine atony and hemorrhage requiring removal of the uterus and treatment of shock. The possible causative factors are reviewed and the opinion offered that widespread adenomyosis of the myometrium interfered with its normal contraction and prevented its response to oxytocic drugs.

REFERENCES

(1) *Stone, M. L.*: Am. J. Obst. & Gynec. **35**: 883, 1938. (2) *Batizfalvy, J.*: Zentralbl. f. Gynäk. **63**: 40, 1939. (3) *Schweitzer:* Ibid. **51**: 938, 1927. (4) *Szenes, A.:* Arch. f. Gynäk. **134**: 546, 1928. (5) *Bumm, E.:* Grundriss z. Studium d. Geburtschilfe, ed. 15, Munich, 1922, J. F. Bergman, p. 350.

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DISCUSSION

DR. MELVIN L. STONE.—In the Laboratory of Gynecological Pathology at Bellevue Hospital we have seen, incidental to routine study of material removed at operation, many instances of adenomyotic foci ranging from minute incursions of the glands of the endometrium into the muscle, to more extensive foci of adenomyosis which are completely removed from the endometrium. These have been noted especially in fibroids and in many other conditions, but we have never seen a case producing uterine atony. We have, however, noted a similar case which I would like to describe to you. The patient in question was a woman of 25 years who had had no pregnancies prior to her admission to Bellevue Hospital in labor. She was at term at the time and was having pains every ten minutes. We examined her and could find nothing very obviously wrong except that she had a very marked cystitis and complained grievously of dysuria because of this. About four or five hours after admission the blood pressure dropped rather markedly, the pulse became imperceptible, the skin became cold and clammy and the uterine contractions ceased. The fetal heart could not be heard. Under the diagnosis of ablatio placentae the patient was subjected to operation. At first glance, when the peritoneal cavity was entered, nothing remarkable was noted. The uterus was distended to the size of a full-term pregnancy and appeared perfectly normal otherwise.

On palpating the uterus posteriorly, however, we felt a cystic mass which we thought was blood clot, inasmuch as there was about 1,000 c.c. of fluid blood in the peritoneal cavity; after removing the fetus, and delivering the empty uterus through the incision, we were rather surprised to find a rupture about 5 cm. in length on the posterior surface of the uterus, through which collapsed membranes were protruding. We removed the uterus and the patient made an uneventful recovery, following transfusions and the usual after-care.

Examination of the uterus from its inner surface revealed a deep crevice in its left side and cornu. This area was ragged and bluish red in color and through it the perforation had occurred. The thickness of the uterine wall throughout the extent of the crevice was about 0.5 cm. in contrast to the thickness of the remainder of the wall which was 3 or 4 cm. This observation verifies the statement which Dr. Molytoff made relative to the destructive effect of endometrial stroma and glands on myometrium.

Microscopic sections, taken through the perforated area, showed a marked decidual reaction which had taken place in islets of ectopic endometrium and throughout the uterus many other such endometrial islands were observed.

It is of interest, as Dr. Sackett stated, that a case such as this was described by Dr. Richardson in 1919 some time before the general recognition of endometriosis as an entity. Dr. Richardson was of the belief that the endometrium, after it had undergone decidual change, possessed some unique power which enabled it to proliferate and invade muscle tissue. It seems, in view of our later knowledge of the subject, that this also was a classical case of endometriosis and that the decidual reaction which he observed was a secondary effect of pregnancy on ectopic endometrial foci.

DR. LEON MOTYLOFF.—It is not generally appreciated that adenomyosis of the uterus is a destructive condition. The endometrial foci in adenomyosis consist of glands and stroma. The glands are usually harmless, but the stroma may be extremely aggressive. It was found by Robert Meyer in 1923 that the stroma of the endometrial islets destroys the myometrium, and he found destruction not only of the interstitial tissue, but also of the most important elements of the muscle cells, the so-called myofibrils, which are responsible for the function of muscle.

Fortunately, not all cases of endometriosis are alike, as is evident from clinical experience. Some of the cases show quite an extensive menorrhagia and others do not. Perhaps the most aggressive types of endometriosis are the recent cases with very cellular stroma. In Dr. Sackett's case the stroma was very cellular which is why it showed such decidual reaction. All the cases that have been reported where the combination of adenomyosis and atony were found, presented such an extensive decidual reaction.

LATERAL PYOCOLPOS, DOUBLE UTERUS, CERVIX, AND VAGINA, WITH ABSENCE OF LEFT KIDNEY*

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(From the Gynecological Service of the Mount Sinai Hospital)

THIS case of lateral pyocolpos, with double uterus, double cervix, and double vagina, associated with absence of one kidney, is being reported because of its clinical interest, and particularly to emphasize the importance of accurate preoperative diagnosis.

The patient, L. M., was a white virgin, 25 years of age. The family history was negative. Menstruation had started at 12½ years, was always regular, occurring every twenty-eight days, profuse in amount, and lasting eight days. There was no intermenstrual bleeding. Dysmenorrhea was present on the first day of each menstruation.

At the age of 17 years, the patient noticed a foul, yellowish discharge. This illness was gradual in onset, and not accompanied by chills or fever. The discharge persisted and increased, particularly before the menstrual flow.

At the age of 24, one year ago, she first experienced pain, and a sensation of heaviness in the left lower quadrant. This interfered with walking, occasionally with sleep. At the time of her menses, there was pain in the right leg. There were no urinary symptoms.

Four months ago she was admitted to another hospital, at which no diagnosis was made, and she was discharged with the recommendation to take douches. She then went to the Consultation Clinic at Mount Sinai Hospital, where it was thought that she might have a complex congenital anomaly, and further hospital investigation was advised. She was admitted to the gynecological service of Dr. Geist, to whom I am indebted for the privilege of investigating this case.

Physical examination showed a young, white woman, not acutely ill, fairly well developed. There were no gross stigmas of a glandular disturbance. The general examination was negative; blood pressure was 96 systolic, 66 diastolic; the hemoglobin was 86 per cent. There were 18,800 white blood cells with 53 per cent polymorphonuclear leucocytes. Urine examination was negative. The Wassermann test was negative, the sedimentation time was one and one-half hours. The vaginal smear showed many leucocytes and cocci in chains.

Pelvic examination showed a virginal introitus. There was a profuse, foul-smelling vaginal discharge. Upon rectal examination, the cervix seemed normal in size. The fundus could not be differentiated. The right adnexa seemed normal. To the left there was a cystic mass, the size of an orange, bulging toward the vagina and extending upward and laterally. This was slightly tender. Capping this mass, there was a second, smaller mass in the left lower quadrant. Pressure upon the cystic mass increased the vaginal discharge.

Intravenous pyelogram failed to show any shadow of the left urinary tract. Methylene blue, given by mouth, did not discolor a gauze strip placed in the vagina. Vaginal smears were negative for tubercle bacilli.

Cystoscopy was performed, at which time the right ureteral orifice was easily catheterized; there was no opening to correspond to the left ureter. Indigo carmine appeared on the right side only. The vagina was inspected with a narrow proctoscope. A cervix was seen, and the os was normal. One-half inch to the left of this there was the opening of a sinus, from which pus exuded. This was of the size of a ureteral orifice and led to a tortuous tract. The right lateral fornix was well defined; the left fornix was apparently absent, the cervix merging into the left vaginal wall. Microscopic examination of the pus aspirated from within the sinus opening showed pus cells and squamous epithelial cells (Fig. 1).

*Presented at a meeting of the New York Obstetrical Society, November 12, 1940.

When the patient began to menstruate several days later, a second vaginoscopy was immediately performed, and blood, mixed with pus, was seen issuing from the sinus opening to the left of the cervical os. At this time, no blood was, as yet, issuing from the cervix itself. The blood from the sinus opening was collected, centrifuged, fixed, and sectioned (Fig. 2), according to the method suggested by Dr. Geist, for determination of menstrual blood. It was reported as consisting of blood, leucocytes, and endometrial epithelium.

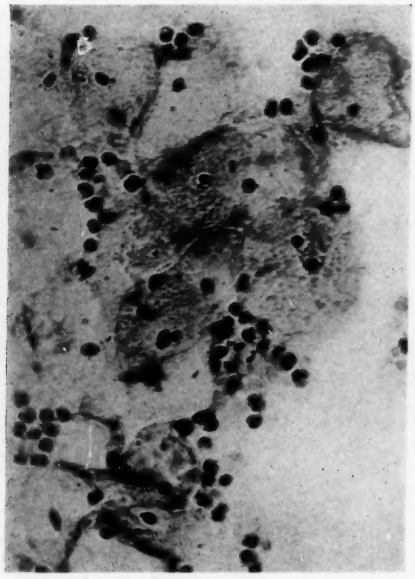

Fig. 1.

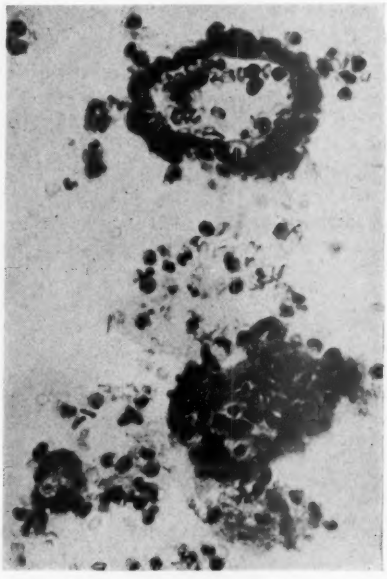

Fig. 2.

Fig. 1.—Secretion aspirated from sinus opening, showing pus cells and squamous epithelium.

Fig. 2.—Menstrual blood and pus aspirated from sinus opening, showing endometrial glands.

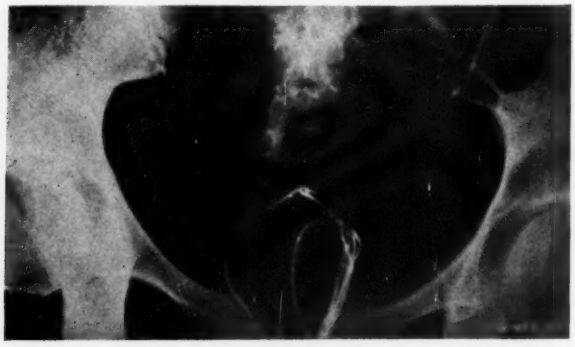

Fig. 3.—A ureter catheter threaded into the orifice in the vaginal fornix, coiled up in the cavity.

On the following day menstrual blood was also seen issuing from the cervix. The hymen was then dilated to admit a speculum, and a ureter catheter was threaded into the sinus opening. X-ray picture showed it to be coiled up in a cavity paralleling the upper three-fourths of the vagina (Fig. 3). Hippuran was injected, and an x-ray picture taken, outlining the cyst (Fig. 4). A sound passed into the cervix showed a uterus deflected to the right side of the pelvis (Fig. 5).

The sinus opening was now dilated with graduated sounds, and the cystic cavity (lateral pyocolpos) regularly irrigated. The discharge diminished rapidly, pain disappeared, and the patient felt greatly improved. When the return from the irrigation became almost clear, operation was performed.

Fig. 4.—A sound is in the right uterus. Hippuran has been injected through the catheter and outlines the atretic left vagina. Some excess hippuran is seen in the right vagina.

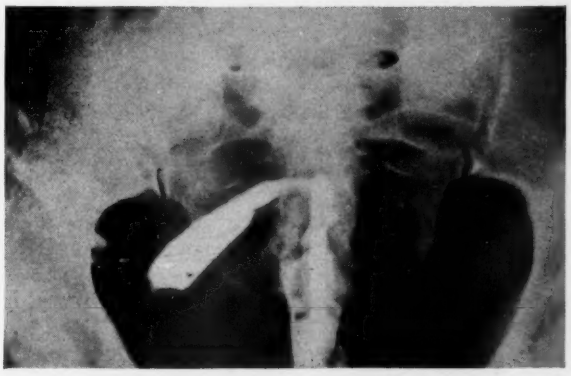

Fig. 5.—Right hysterogram showing position of the right uterus and the tube. The uterotubal angle is well demonstrated.

Operation.—Under general anesthesia, the vault of the vagina was exposed, a cannula inserted into the sinus opening, and the lateral pyocolpos flushed with saline solution. When the return was clear, the cavity was distended with fluid by means of a cannula fitted with an appropriate obdurator. The most inferior portion of the distended cavity, one-half inch above the hymen, was aspirated with a 20-gauge needle, and a window made at this point. A good portion of the septum between the sinus opening and this window was then excised, and complete drainage established. The vagina, now converted into a single space, was packed.

Pathologic examination of the wall showed "fibromuscular septum covered on both sides by squamous epithelium" (Fig. 6).

Within a week all discharge had stopped. The wall of the cyst now had the appearance of normal vaginal epithelium. To the left of the previously noted

cervix (right), at a slightly higher level, a second cervix was seen, about two-thirds as large as the right cervix. Its os was patent, easily sounded, and the corresponding uterus was turned to the left. The stump of the septum was between the two cervices.

Cannulas were inserted into both uteri, and simultaneous bilateral hysterograms were made (Fig. 7). This proved the diagnosis of double uterus, double cervix, and double vagina with lateral pyocolpos due to atresia of the lower end of the left vagina, the anomaly being accompanied by the complete absence of the left kidney.

Fifteen days postoperative, the patient began to menstruate, and menstrual blood was seen issuing from both cervices. At this time, both uteri were easily palpated, freely movable, and there were no adnexal masses. The patient was discharged completely well three weeks after operation.

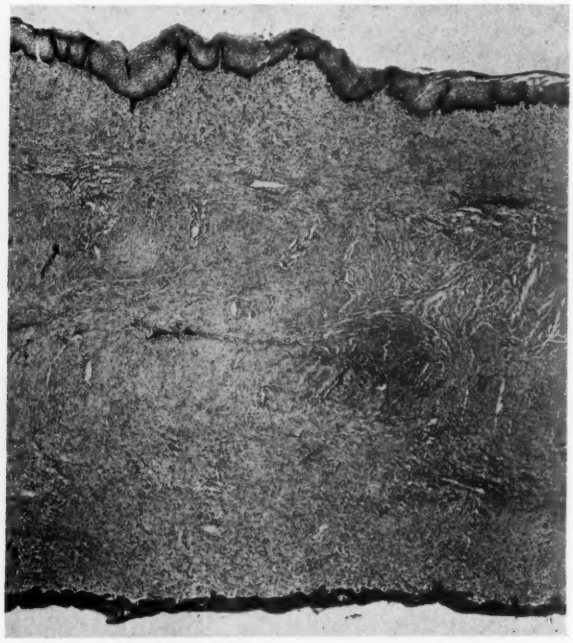

Fig. 6.—Resected septum showing fibromuscular septum lined on both sides with vaginal epithelium.

Follow-up examinations at frequent intervals for over one-half year showed the patient in excellent health, symptom-free, without vaginal discharge. The introitus was normal. A small ridge, 0.5 cm. thick, was present along the posterolateral wall. The mucosa of the left side of the vagina was normal. The cervices appeared normal, and the uteri seemed normal in size. There was no adnexal mass or tenderness.

The case cited is one of failure of complete fusion, with an incomplete breaking through of the left vagina. Arrests of development at this period have the highest correlation with kidney anomalies, including absence of one kidney supposedly due to the impossibility of the ureter bud meeting the definitive kidney anlage.

The clinical picture of the anomaly seen in our patient, as described by numerous authors, is quite characteristic. The patent half of the vagina seems quite normal, although somewhat narrow. The uterus appears to be pushed to one side. To the other side, there is felt a cystic mass extending toward the vulva, and bulging into the normal vagina. In most cases, the cystic mass simulates a low-lying intra-abdominal cyst, and is often capped by a second mass

which proves to be the uterus. Not infrequently, a small communication in the upper part of the septum between the two vaginas permits more or less intermittent discharge of blood or pus.

The diagnosis, however, was not made preoperatively in the majority of cases. As a consequence, a great many of the reported cases were diagnosed only following laparotomy or extensive vaginal dissections.

Jaschke and Pankow in 1933 were enabled to make the diagnosis preoperatively by finding squamous epithelium in the secretion. They emphasized the difficulty in diagnosis, and considered a differential diagnosis between this condition and parametrial abscess almost impossible.

In many instances, quite unnecessary hysterectomies were performed, and equally unnecessary total excisions of the supposed vaginal cysts. Obviously, the procedure of choice is the simple one of extirpating a large portion of the septum, preferably after preliminary cleaning up of infection.

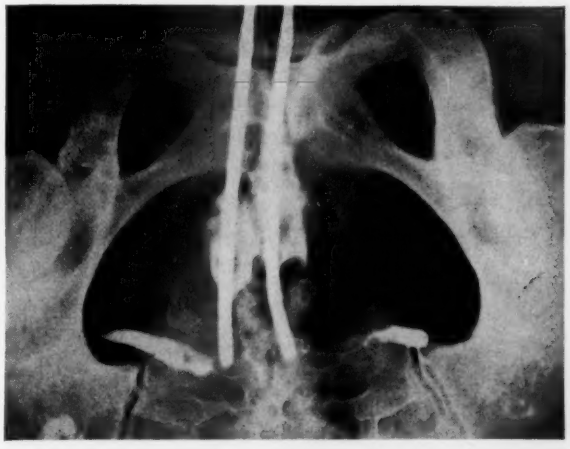

Fig. 7.—Double hysterogram showing both uteri, both tubes. The uteri are laterally placed. The cervices are outlined by hippuran in the vagina, the right at a slightly lower level than the left.

The condition should be suspected in the presence of lateral vaginal cystic masses, or discharges of an obscure nature from vaginal sinuses. The swelling does not always parallel the side of the vagina, and often runs a semispiral course, arising posteriorly and bulging into the abdomen and above Poupart's ligament. This is one of the factors that contributes to difficulty in diagnosis and is misleading.

Once the possibility of such a condition is entertained, we have at our disposal adequate measures to investigate such a case completely. These include, in addition to the ordinary gynecologic examination, the study of the secretion from such sinuses, the catheterization of the pockets, x-ray study with contrast media, and x-ray examination of the uteri. An apparently complex technical problem can thus be converted into a very simple one.

The differential diagnosis from other vaginal cysts, including Gärtner's cyst and cysts of the vagina due to misplaced ureters, is made easy.

All such cases, as well as all other anomalies of the genital tract, should have the benefit of a urologic investigation, including intravenous pyelography, because of the surprisingly frequent association with the absence of one kidney. Over one hundred cases of this association have been reported. According to Ballowitz, in 213 cases of absent kidney, there were 71 females, of whom 41 had anomalies of the genitalia. The frequency of absent kidney is about 1 in 3,000. Up to 1916, 94 cases of absent kidney are in the literature, collected by W. Reusch. This is of scientific interest, and also of clinical importance from the

standpoint of possible injury to the remaining ureter as a result of misguided operative interventions.

The etiology of the infection which converts a lateral hematocolpos into a pyocolpos is not always clear. The stagnation of menstrual blood furnishes an excellent culture medium, and the opening in the septum, primary or secondary to rupture or manipulation, may furnish the point of entry of bacteria. In most instances, the secretion had a foul odor. This was true in our own case.

SUMMARY

1. A case of lateral pyocolpos is described, in which there was a double vagina, double cervix, and double uterus, with atresia of the lower end of the left vagina. This genital anomaly was associated with the absence of the left kidney.

2. Complete diagnosis of the condition preoperatively facilitated the extremely simple therapy.

3. Treatment recommended is preliminary cleaning up of the infection by irrigation, followed by removal of the septum between the two vaginas.

4. Points of importance in the investigation are the examination of the secretion from the lateral cyst, the use of contrast media in the pyocolpos and uterus, the determination of endometrium in the menstrual blood aspirated from the cavity, and the investigation of the genitourinary tract.

I wish to express my thanks to Dr. Geist for the privilege of investigating this case.

HYDATIDIFORM MOLE FOLLOWED BY CHORIONEPITHELIOMA*

EDWARD FRANCIS MCLAUGHLIN, M.D., PHILADELPHIA, PA.
(From the Germantown Hospital)

IT IS striking that the conditions of hydatidiform mole and chorionepithelioma are reputedly of such infrequent occurrence, and the sequence of epithelioma following mole is of even more rare occurrence.[1-6] I believe that a greater number of these tumor cases exist than is generally assumed, and that they are treated in the surgical wards of hospitals where gynecology is included under surgery. Two such cases, the occurrence of which might otherwise have passed unrecorded, are reported herewith.

CASE 1.—E. A. (20955), a colored woman, aged 38 years, was admitted to the Surgical Service of Germantown Hospital Jan. 29, 1936. The relevant portion of her history is as follows: She had missed four periods, was believed to be pregnant, and began to bleed. The diagnosis was "incomplete abortion." She was curetted and large amounts of grapelike masses were obtained which were grossly and microscopically diagnosed "hydatidiform mole." Five days later the patient was reoperated upon and a subtotal hysterectomy, bilateral salpingectomy, and right oophorectomy were done. The uterus was slightly larger than normal, the right ovary being cystic. The left ovary (not removed) appeared to be normal. The pathologic report was as follows: "Uterine canal is soft and boggy and occupying half of the fundus is a large irregular mass of soft friable tissue mixed with considerable blood clot. This appears to have penetrated the endometrium in several places."

Microscopic sections of the uterus revealed a "chorionephithelioma, early with slight penetration" and "chronic interstitial oophoritis with corpus luteum cyst and luteoma." No ovarian metastases were seen.

*Presented at a meeting of the Philadelphia Obstetrical Society, January 2, 1941.

The patient had an uneventful convalescence. Qualitative Friedman tests were done one month and three months after operation and were negative. The patient is well and has negative pelvic findings four years after her discharge.

CASE 2.—C. T. (24534), white, married, was admitted Dec. 20, 1938, to the Surgical Service at Germantown Hospital giving the following story. Her last regular period was two months previous. She noticed a mass in her abdomen which had increased in size, and two weeks before admission vaginal bleeding began and continued off and on, being at first slight, then becoming heavier two days before entering the hospital. Examination showed a mild generalized jaundice, icterus index being 42. Abdominal palpation revealed an irregular mass extending up to the mid-epigastrium and an "irregular attached mass extending almost to the costal margin on the left." Vaginal examination showed the uterus to be continuous with the mass previously described. Red blood count was 1,970,000; Hg, 30 per cent. A diagnosis of pregnancy was made with the possibilities of (1) incomplete abortion; (2) threatened abortion; and (3) possible hydatid degeneration. On Dec. 22, 1938, a qualitative Friedman test was positive. On the same day after proper preparation (blood, etc.), a curettage was done and typical molar tissue recovered. This was reported pathologically as "benign hydatidiform mole" but a later section showed some active proliferation of cells, but no uterine tissue was included in this section so invasion could not be reported upon.

The patient improved rapidly. The uterus was reduced in size. On Jan. 6, 1939, fifteen days after operation a qualitative Friedman test was positive. Examination on the nineteenth postoperative day disclosed a uterus still about twice normal size and a questionable mass in the right side. Operation was advised but the patient refused and went home. Five days after discharge she began to have abdominal pains and noticed a purulent vaginal discharge. She was re-admitted three weeks after leaving the hospital or forty days after her curettement. At this time the uterus had again enlarged somewhat and the abdominal masses, now bilateral and extending up to the umbilicus, could easily be felt. On Feb. 1, 1939, a total hysterectomy and bilateral salpingo-oophorectomy were done by Dr. S. D. Weeder. The uterus was found slightly enlarged but otherwise normal. Both ovaries were distended to a diameter of about eight inches with large cysts, hemorrhagic in some sections. Pathologic examination showed these to be lutein cysts. They contained fluid rich in prolan. The opened uterus had some adherent and penetrating molelike tissue at the upper left pole. In the upper pole was a quantity of necrotic material. Microscopic diagnosis: "hydatidiform mole and chorionepithelioma."

The patient had an uneventful convalescence. One month and one-half after the hysterectomy, a qualitative Friedman test was negative. The patient has refused further visits but is known to be well, symptom free and working at present, two years later.

DISCUSSION

These two cases serve well as texts for a brief discussion. The first case illustrates four points. First the belief held by some that the finding of a mole *ipso facto* calls for a hysterectomy to prevent the growth or spread of the more malignant tumor. If chorionepithelioma is as

malignant as it has been pictured, there is some justification for this stand. This feeling is more understandable too when the patient is near the menopause as was true here. Certainly the decision to re-operate proved fortunate in this instance. A second point is the fact that the operator felt safe in leaving a normal appearing ovary, and time proved he was right in so doing. Third, microscopic sections of the cystic ovary showed no evidences of metastases, adding to the accumulated evidence which tends to show that metastases or extensions from uterus to ovary are rare or never occur. Fourth, while used in an elementary way, the two successive negative qualitative Friedman tests added assurance to the belief that the tumor had been completely removed.

The second case also brings up some interesting points: the use of biologic tests, the value of histologic sections, and the soundness of clinical observations. The qualitative Friedman test done before curettement simply indicated the presence of pregnancy tissue and nothing more. The same test, though positive, taken two weeks after curettement meant nothing because slowly dissolving benign chorionic tissue might still be giving a positive qualitative test. It might even be giving a very high quantitative prolan reading at this time. To base one's decision to do a hysterectomy on persistently positive qualitative Friedman tests in the period immediately following molar evacuation will mean sacrificing of many normal uteri. If these biologic tests are to have value, they must be quantitative, must be taken at frequent intervals, and the values plotted on a graph.[7-10] A steadily falling prolan curve bespeaks benign tissue (Payne); a rising curve, the reverse. Return to normal usually takes eight to twelve weeks.[11, 12]

The curetted tissue was not of great help because no specimen included the molar—uterine junction, and invasion could neither be demonstrated nor ruled out. To secure the most desirable tissue, direct excision by hysterectomy[3] or a careful selection of the last of the curetted fragments must be done. If a suitable specimen can be secured, histologic diagnosis of chorionepithelioma is feasible despite the opinions of many to the contrary.[9, 10, 12] Chorionepithelioma was readily diagnosed in the sections taken from the extirpated uteri and the diagnosis confirmed by more than one competent pathologist.

Clinical findings really brought this patient to her second and life-saving operation. Persistent, then enlarging, ovarian masses, and re-enlargement of the uterus are very strongly suggestive, in this situation, of the presence of actively growing chorionic tissue. Another clinical sign, not noticed here, is the reappearance of uterine bleeding. Where prolan estimation and histologic section are not available, these clinical signs alone would call for a second curettement, a hysterotomy, or possibly even a hysterectomy.

The operator in Case 2 held the opinion that if malignancy be present in the uterus then both adnexa should be completely removed, so that these possible sites for extension or near-by metastases may be eliminated. Whether these adnexal structures appear normal or abnormal is beside the point. So the huge cystic ovaries, made so by the many lutein cysts whose fluid is rich in prolan, were removed. Many gynecologists believe such ovaries are completely benign and will return to normal after the stimulator of prolan production, the chorionic tissue, is removed. All[9, 13, 14] admit of the possibilities of hemorrhage from and torsion of such cystic ovaries. In the present instance, histologic section of the

removed ovaries showed no malignancy, again adding to the evidence that involvement of these structures by chorionepithelioma is rare.

The dispute over the proper course to pursue with the ovaries brings up the most important question on the whole subject of chorionepithelioma. Just how malignant is this tumor? On the one hand is it the rapidly fatal blood metastasizing super-cancer? Or on the other, is it the tumor whose distant and widespread metastases will disappear after the parent tumor is excised? Is it the tumor which has even been reported to have spontaneously regressed and disappeared itself along with its metastases? Between these two extremes the answers lie for there must either be grades of malignancy as Ewing[15] believes or grades of host resistance as Montgomery[16] believes.

I desire to express my appreciation to Drs. E. B. Hodge and W. B. Swartley for permission to report these cases.

REFERENCES

(1) *Curtis, A. H.:* Textbook of Gynecology, Philadelphia, 1930, W. B. Saunders Co. (2) *DeLee, J. B.:* The Principles and Practice of Obstetrics, Philadelphia, 1925, W. B. Saunders Co. (3) *Schuman, E. A., and Voegelin, A. W.:* Am. J. Obst. & Gynec. **33:** 473, 1937. (4) *Sherman, J. T.:* Am. J. Surg. **27:** 237, 1935. (5) *Mathieu, A.:* Am. J. Obst. & Gynec. **57:** 654, 1939; also Novak's discussion. (6) *Mathieu, A.:* Surg., Gynec. & Obst. **64:** 1021, 1937. (7) *Zondek, B.:* J. A. M. A. **108:** 607, 1937. (8) *Brindeau, A., Hinglais, H., and Hinglais, M.:* Gynéc. et obst. **40:** 208, 1939. (9) *Mathieu, A.:* Surg., Gynec. & Obst. **64:** 1121, 1937. (10) *Payne, F. L.:* Paper unpublished. (11) *Kimbrough, R. A., Jr.:* Am. J. Obst. & Gynec. **28:** 12, 1934. (12) *Mazer, C., and Goldstein, L.:* Clinical Endocrinology in the Female, Philadelphia, 1932, W. B. Saunders Co. (13) *Meigs, J. V.:* In discussion of Mathieu.[5] (14) *Smiley, J., and Clements, A. B.:* Am. J. Obst. & Gynec. **10:** 471, 1940. (15) *Ewing, J.:* Quoted by Wilson, K. M.: Am. J. Obst. & Gynec. **38:** 824, 1939. (16) *Montgomery, T.:* In discussion of Mathieu.[5] Am. J. Obst. & Gynec. **57:** 654, 1939.

DISCUSSION

DR. EDWARD SCHUMAN.—Lutein cysts of the ovary, accompanying hydatid moles or chorionepithelioma, represent a lutein reaction to the tremendous amount of gonadotropic substance elaborated by the chorionepithelioma. There has been some question in my mind as to whether the ovaries should routinely be removed in the presence of this disease. They are very rarely the seat of metastasis and there usually remains some doubt about the malignancy of chorionic tumors at the time of operation.

With regard to the fallibility of the hormone tests in the presence of mole or chorionepithelioma, Dr. Voegelin and I reported a case in which Aschheim-Zondek tests were negative for something over a year, while the patient was suffering from chorionepithelioma. These tests did not become positive until a month before the patient's death.

Itoh, R.: Determination of Sex of Fetus, Zentralbl. f. Gynäk. **64:** 1302, 1940.

The author claims successful prediction of sex in 15 cases. Using the maternal urine, Itoh extracted it with acetone and ether, combining the resulting fraction with an acetone-ether extracted fraction of dog testes. The effect of a proteolytic ferment, which the author claims is secreted by the fetal testes, will be to elevate the amino-nitrogen content of the above mixture, while a low aminonitrogen value will be obtained in the case of female fetuses.

R. J. Weissman

STETHOGRAM AND RECORDED DISC OF FETAL HEART SOUNDS IN A TWIN PREGNANCY

ARTHUR L. SMITH, A.M., M.D., F.A.C.P., LINCOLN, NEB.

ONLY a few have succeeded in making photographic records of fetal heart sounds and in some of these the vibrations are very indistinct. Orias and Braun-Menendez[1] state that the recording of fetal heart sounds is very difficult and this explains why so few such studies have been made. In their book on heart sounds two stethograms of fetal hearts made by Pereira are shown and these are very good. Hofbauer and Weiss[2] in 1908 and Beruti[3] in 1923 succeeded in making a few photographic records of fetal heart sounds but the results were very unsatisfactory. Lian, Golblin and Minot[4] in 1938 made graphic records of fetal heart sounds (number not stated) and also cut a few discs. Smith and Hervert[5, 6] in 1940 succeeded in making fetal stethograms and recording reproducible fetal heart sounds on discs in 52 cases. Dressler and Moskowitz[7] in 1941 simultaneously recorded fetal stethograms and electrocardiograms (by the Strassman technique) in 40 cases.

In none of these reports has the recording of twin fetuses been mentioned. In the review of all the medical literature on this subject, no recordings of a twin pregnancy by stethograms or phonographic discs have been found. However, Bell[8] has reported the taking of fetal electrocardiograms in two cases of twin pregnancies, one of these yielding fetal deflections while the other was unsuccessful. Electrocardiograms were taken on 33 pregnant women, and in 10 of these fetal heart R-waves were registered.

CASE REPORT

Primipara, 24 years of age, was admitted to the hospital on Oct. 14, 1940. On physical examination a diagnosis of twins was made and two fetuses were seen in the roentgenogram. The first fetus (No. 1) filled the right side of the abdomen, the head was in the pelvis and the back on the right. The head of the second fetus (No. 2) was seen in the left lower abdomen and the back above it was curved laterally.

The heart sounds of the first fetus were easily heard through the stethoscope in the right lower abdomen, but the sounds of the second fetus could not be found. So the problem was to know whether the second fetus was living or not.

Fetal stethograms, cardiophonograms, and electrocardiograms with maternal electrocardiograms and pulse were taken simultaneously. Following this, the maternal heart sounds, electrocardiogram, and polygram were recorded at the same time.

The stethograph used to photograph the heart sounds has been described by Lockhart[9] and the cardiophonograph (Fig. 1) employed to cut the discs of reproducible heart sounds was developed by the author.[10, 11]

The fetal electrocardiographic technique followed was that described by Strassman and Mussey.[12, 13]

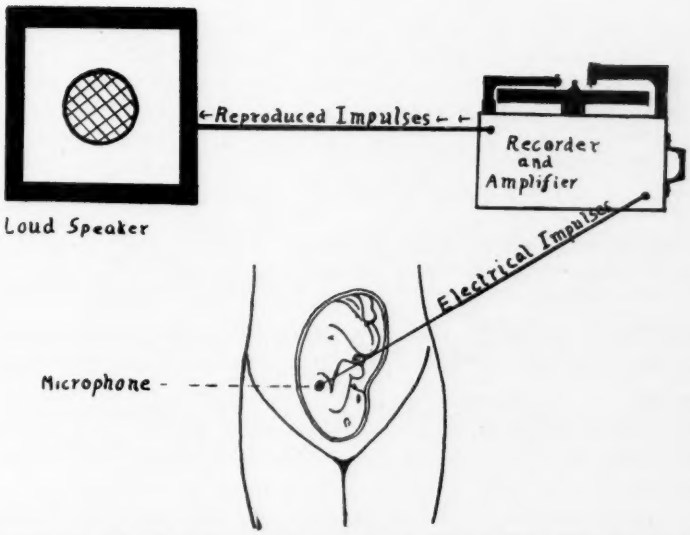

Fig. 1.—Diagram of method of making recorded discs and auditing heart sounds from records or directly from the fetal heart.

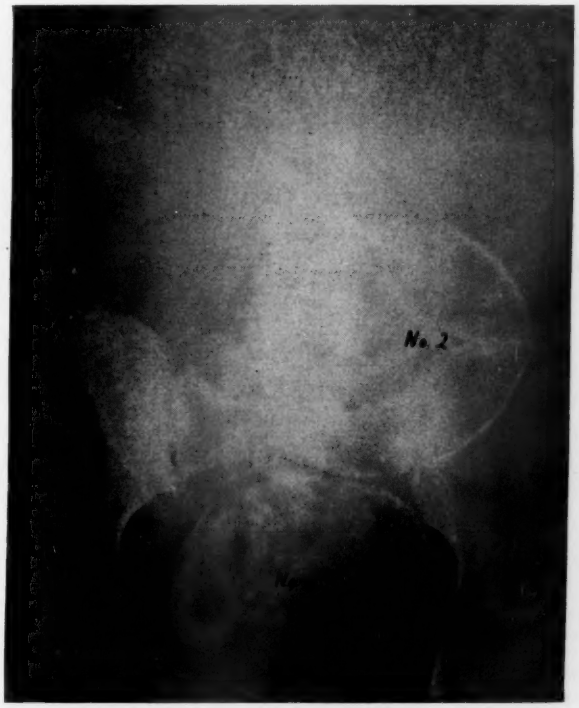

Fig. 2.—Roentgenogram of twin fetuses. No. 1 right lower and No. 2 left upper.

STETHOGRAMS

First Fetus (No. 1).—These heart sounds were taken through the lower right abdominal wall and over the back of the first fetus. The second sounds were of greater intensity than the first. The first sounds were made up of two vibrations, while the second consisted of four cycles and appeared to be split. Systoles varied in duration from 0.19 to 0.22, and diastoles from 0.23 to 0.26 second. The rhythm which varied somewhat was of sinus origin and the rate averaged 129 per minute.

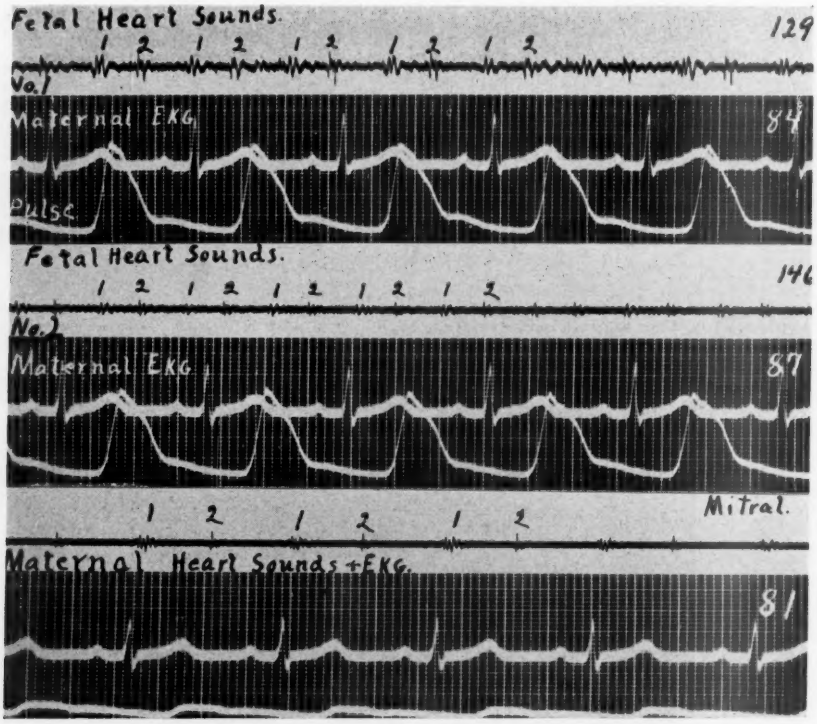

Fig. 3.—*Upper.* Heart sounds of fetus No. 1 with a rate of 129. Maternal electrocardiogram (Lead I) and pulse. *Middle.* Heart sounds of fetus No. 2, the heart rate is 146. Maternal electrocardiogram (Lead I) and pulse. *Lower.* Maternal mitral heart sounds, electrocardiogram (Lead I), and pulse. Each group is taken simultaneously.

Second Fetus (No. 2).—This stethogram was taken over the midlateral left abdomen and the back of the second fetus. The sounds were of low intensity, while the vibrations were slow in the first (1) and more rapid in the second (2). The duration of systoles was 0.17 to 0.19, and diastoles 0.21 to 0.22 second. The sinus rhythm was almost regular, while the rate averaged 146.

Mother.—The heart sounds were of low and about equal intensity over the apex. The first was of much longer duration than the second. No murmurs were heard, and the diastole (0.38 second) was longer than the systole (0.32 second). The rate varied from 81 to 87.

ELECTROCARDIOGRAM AND POLYGRAM

The electrocardiogram and pulse were those of the mother and were taken simultaneously with the heart sounds in each case. No fetal waves were seen in the electrocardiogram.

RECORDED HEART SOUNDS

Those of the first fetus when reproduced were loud and clear and of equal intensity, the rhythm varied considerably, and a soft uterine souffle could be heard. The movement of the fetus was clearly audible.

The sounds of the second fetus were partly neutralized at times by the uterine souffle. They were softer in character than the first and varied in rate and rhythm. Movement of intestinal contents could be heard at times.

In the maternal sounds the first was of greater duration than the second, but they were about equal in intensity. No murmurs were audible, but the respiratory sounds were distinctly heard.

A diagnosis of live twin fetuses with normal hearts was made.

Two normal babies were born on Nov. 1, 1940, and the heart rate of No. 1, which was born first, was slower than that of No. 2.

SUMMARY

A stethogram of twin fetuses and the disc recording of these heart sounds, which could be audited when desired, are reported.

A twin pregnancy in which there was a question of viability of one fetus is described.

The stethogram and recorded disc of the twin fetal heart sounds made the positive diagnosis of two live fetuses, and this was confirmed by the birth of two normal babies.

This is believed to be the first stethogram and disc recording of twin fetal heart sounds reported in medical literature.

I wish to thank Dr. W. J. Hervert for the opportunity to study this case.

REFERENCES

(1) *Orias, O., and Braun-Menendez, E.:* The Heart Sounds in Normal and Pathological Conditions, Oxford University Press, 1939, p. 135. (2) *Hofbauer, J., and Weiss, O.:* Zentralbl. f. Gynäk. **22:** 429, 1908. (3) *Beruti, J. A.:* Rev. espan. obst. y ginec. **8:** 516, 1923. (4) *Lian, C., Golblin, V., and Minot, G.:* Bull. Soc. Gynec. et d'obst. **27:** 423, 1938. (5) *Smith, A. L., and Hervert, W. J.:* AM. J. OBST. & GYNEC. **40:** 102, 1940. (6) *Smith, A. L.:* Read at the Sixteenth Scientific Sessions of American Heart Assoc., June 7, 1940. (7) *Dressler, M., and Moskowitz, S. N.:* AM. J. OBST. & GYNEC. **41:** 775, 1941. (8) *Bell, G. H.:* J. Obst. & Gynaec. Brit. Emp. **45:** 802, 1938. (9) *Bierring, W. L., Bone, H. C., and Lockhart, M. L.:* J. A. M. A. **104:** 628, 1935. (10) *Smith, A. L.:* The Merck Report, April, 1941, p. 6. (11) *Smith, A. L.:* Medical Times **69:** 243, 1941. (12) *Strassman, E. O., and Mussey, R. D.:* AM. J. OBST. & GYNEC. **36:** 986, 1938. (13) *Strassman, E. O.:* Proc. Staff Meet. Mayo Clinic **11:** 778, 1936.

134 SOUTH THIRTEENTH STREET

Peller, E.: Sebaceous Glands in the Cervical Mucosa, Zentralbl. f. Gynäk. **64:** 1258, 1940.

A 40-year-old woman complained of a yellowish, occasionally bloody vaginal discharge of four weeks' duration. Colposcopic diagnosis of sebaceous glands in the cervical mucosa was made and confirmed microscopically. Small yellow spots could be seen over the portio as the source of the discharge, the glands appearing as small cystic elevations. The author uses colposcopy routinely.

R. J. WEISSMAN

THECA CELL TUMOR OF OVARY AND ENDOMETRIAL CARCINOMA

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THECA cell tumors of the ovary are comparatively rare, since Dockerty in 1940 was able to collect only 25 cases from the literature, to which he added 10 more. In the same year, 6 more cases were reported by various authors.

The first 6 examples of this tumor were described by Loffler and Priesel in 1932, under the name "fibroma theco-cellulare xanthomatodes." Undoubtedly there are more cases which have gone unrecognized, possibly due to the close similarity of the histologic picture of this tumor to the ordinary fibroblastoma.

Traut and Butterworth studied a group of mouse ovarian tumors which had been artificially produced with x-rays by Furth and Butterworth. They were able to trace the origin of theca cell, granulosa cell, and lutein cell tumors. There was also definite evidence that the tumors were physiologically active. It has also been shown by various investigators that blood of patients with theca cell tumors contained increased amounts of estrin.

The following case interested us because of the associated adenocarcinoma of the endometrium. Most of these tumors produce uterine bleeding, which results from endometrial stimulation caused by estrin secreted by the tumor. However, when such a tumor is found in individuals who have not reached the menopause, there is usually amenorrhea. In the following case we feel that the association of the two neoplasms is more than coincidental.

CASE REPORT

L. K., a 72-year-old female, was referred to the hospital because of occasional small amount of vaginal bleeding over a period of two years. Except for an occasional heavy, bearing-down sensation in the pelvis, there had been no other symptoms. The bleeding had never been profuse, but had been rather constant. During this time she gained a small amount in weight, and except for past history of occasional attacks of arthritis, her medical history was negative. Menstrual history was normal and uneventful. The menopause occurred at the age of 55 years, and there had been no bleeding up until two years ago.

Physical examination showed a well-developed and well-nourished white woman of 72 years, showing atrophic arthritic changes of the joints of hands, wrist, and ankles. Heart and lungs were normal; thyroid was not enlarged. Breasts were well-developed, pendulous, slightly atrophic; no masses were palpated. Abdomen was obese, soft, and no masses or tenderness was made out. Pelvic examination: vagina atrophic; there was some whiteness about the labia, suggestive of leucoplakia. The cervix showed a very small polyp protruding from the external os. The

uterus was in third degree of retroversion, slightly and irregular enlarged. In the right vault there was an indefinite mass. On May 10, 1940, under gas anesthesia, the cervical polyp was removed and the base cauterized. At that time an attempt was made to dilate the cervix, but no opening could be found from the internal os into the uterus. The patient was discharged from the hospital May 17, 1940, and told to report if she had any more bleeding. On July 24, 1940, she was readmitted to the hospital because of continued vaginal bleeding. On July 27, under gas-ether anesthesia, the abdomen was opened through a low midline

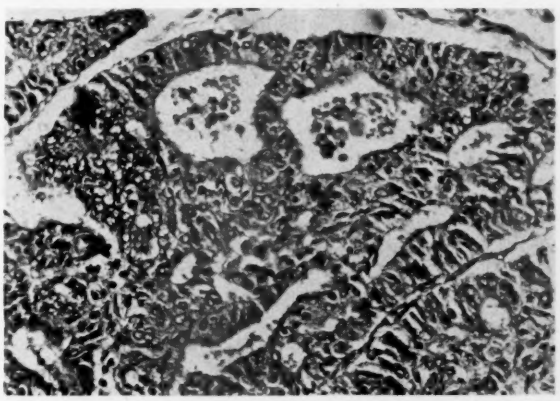

Fig. 1.—High power photomicrograph of the endometrial tumor shows acini lined by columnar epithelium.

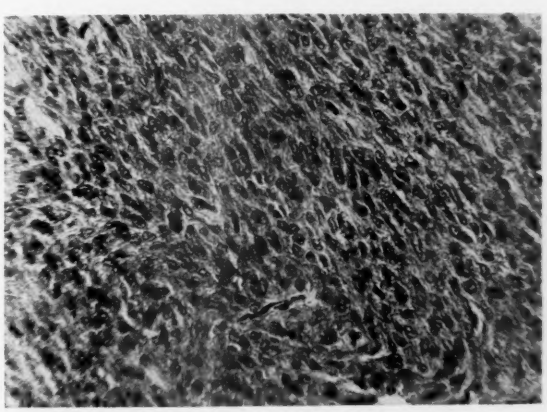

Fig. 2.—High power photomicrograph of the ovarian tumor stained with hematoxylin and eosin. A characteristic field composed of spindle-shaped cells. Lipoid droplets not apparent with this stain.

incision extending from the pubis to the umbilicus. The gall bladder was palpated and found to be filled with small stones. The uterus was approximately four times normal size for a woman of this age, and the left ovary was detached, enlarged, and cystic, lying beneath the uterus in the left portion of the cul-de-sac. This ovarian tumor was apparently without any major blood supply. It was easily removed, after dissecting away the adhesions by both sharp and blunt dissection. The right tube, ovary, and uterus, including the cervix, were then removed. The vagina was closed with interrupted sutures and suspended by the round liga-

ments. Raw areas were peritonized. The patient made a normal convalescence and was discharged from the hospital Aug. 8, 1940. Since then she has returned to our tumor clinic, and has been doing very well. She has no pelvic symptoms and pelvic examination has been negative throughout.

Pathologic Examination.—Uterus was enlarged, measuring 8 cm. in length, 7 cm. in width, and 3 cm. in depth. The uterine cavity was occupied by a soft, friable, reddish-purple mass, which was attached by a wide base to the endometrial surface. The mass extended for some distance into the myometrium. In addition, there was a small intramural fibroid 2 cm. in diameter. The right ovary had been replaced by a solid, encapsulated, bright yellow, firm mass measuring 4 by 2 by 2 cm. The left ovary measured 14 by 1 by 1 cm. and contained small follicle cysts.

Microscopic examination of the uterine tumor revealed structure composed of irregular glands lined by low columnar cells (Fig. 1), which showed no evidence of secretory activity. The interglandular stroma was scant and almost absent in places. The tumor invaded the myometrium for a short distance. The adjacent endometrial glands were greatly and irregularly dilated, but there was very little stromal activity.

The ovarian tumor (Fig. 2) was composed of closely-packed, small, elongated or oval cells, which occasionally are arranged in wide, sweeping bundles, and elsewhere form small interlacing networks. The intercellular substance was pale and scant. Fine fibrils were seen with Mallory's phosphotungstic acid stain and Masson's trichrome. Scarlet R brings out the numerous fine, fat droplets in practically all cells and stroma.

Comment.—This case is characteristic of previously reported theca cell tumors of the ovary, and is of special interest because of the associated endometrial carcinoma. While it is not possible to prove that the ovarian tumor was the etiologic agent responsible for the uterine tumor, our knowledge of theca cell tumors and their similarity to granulosal cell tumors would lead one to believe that the physiologic hyperplasia of the endometrium has progressed to a neoplasm. It is generally accepted that the majority of granulosal cell tumors and theca cell tumors secrete estrin. They do cause stimulation of the endometrium, with resultant bleeding. Granulosal cell tumors may occur at any age, while theca cell tumors are usually found after the menopause. In 10 cases of theca cell tumors of the ovary reported by Dockerty, carcinoma of the endometrium was encountered once. This same author found 3 carcinomas of the endometrium in 32 cases of granulosal cell tumors of the ovary.

A case of theca cell tumor of the ovary with an associated carcinoma of the endometrium is presented, in which we feel that it is reasonable to assume that the ovarian tumor played a major role in the production of the uterine tumor.

REFERENCES

(1) *Dockerty, M. B.:* Am. J. Obst. & Gynec. **39:** 434, 1940. (2) *Loffler, E., and Priesel, A.:* Beitr. z. path. Anat. u. z. allg. Path. **90:** 199, 1932. (3) *Traut, H. F., and Butterworth, J. S:* Am. J. Obst. & Gynec. **34:** 987, 1937.

INTESTINAL OBSTRUCTION FOLLOWING THE BALDY-WEBSTER SUSPENSION OF THE UTERUS

WILLIAM BICKERS, M.D., RICHMOND, VA.

FREQUENT reference is made in medical literature to intestinal obstruction occurring after suspension operations, but actually there are comparatively few cases reported. Usually this complication is mentioned by the authors only to prove that one type of operation is superior to another. The Baldy-Webster technique is used by many gynecologists on the assumption that it leaves no potential hernial openings in the peritoneal cavity and thus has a certain advantage over other operations. This may be true. The literature does not contain a sufficiently comprehensive study of this very important problem to permit us to draw any conclusion as to which operation is least likely to cause subsequent intestinal complications. In the present state of our knowledge, this most important question cannot be answered. Since it is true, however, that many surgeons use the Baldy-Webster technique on the assumption that it eliminates this potential hazard, the following cases of mechanical obstruction through hernial openings in the broad ligaments are reported.

CASE 1.—D. D., aged 31 years, white, was the mother of three living children. Prior to her last pregnancy the patient had a Baldy-Webster suspension of the uterus for an uncomplicated retroversion. Six months after the operation she became pregnant, enjoyed an uneventful gestation, and delivered a normal female infant at term, following a short, spontaneous labor. The operation did not in any way complicate the pregnancy. Three months after the delivery she was seen one evening with acute pain in the left lower quadrant which was soon accompanied by vomiting. Pelvic examination revealed a normal size uterus in anterior position and a movable, nontender mass in the region of the right adnexa. The patient insisted that her pain was on the left, but in spite of her persistence, a diagnosis of right ovarian cyst with twisted pedicle was made. No mass could be palpated on the left. The patient was removed to the hospital and prepared for operation. On opening the abdomen, a pseudomucinous cyst of the right ovary which was not twisted could be seen and this was removed. Just to the left of the uterus and below the ovarian ligament there was an opening in the left broad ligament through which 10 cm. of the ileum was herniated. The bowel was strangulated but in good condition. The hernia was reduced and the broad ligament opening closed after freeing the round ligament on that side and plicating it in front of the closed opening on the anterior leaf of the broad ligament. Inspection of the opposite side showed a firm adhesion of the round ligament to the broad ligament; no opening could be seen, and it was left in place.

CASE 2.—C. S., aged 19 years, virgin, had a Baldy-Webster suspension at the age of 17 for a retroversion which was thought to be the cause of severe dysmenorrhea. The operation corrected the displacement but not the dysmenorrhea. When the patient was seen two years after the operation, she gave a history of two attacks of acute abdominal pain accompanied by vomiting which had been treated with bed rest and sedation. She stated that in both instances the pain had come on suddenly and left her with the same celerity. It was after the second attack that the patient was referred to me for a gynecologic opinion on the cause of this pain. Examination revealed nothing but a well suspended uterus and normal adnexa. Two days after this examination the patient had another acute attack of pain and at this time the diagnosis was apparent. Clinical signs of hyperperistalsis, pallor, rapid pulse, and intractable vomiting were present. On pelvic examination a mass was palpable in the region of the left parametrium. At operation an interesting situation presented itself. There was an opening in the posterior leaf of the left broad ligament at the site of the round ligament exit through which a loop of ileum had herniated into the left broad ligament and had dissected between the leaves for a distance of several centimeters. The anterior leaf was firmly adherent to the round ligament and presented no opening. The hernia was reduced and the suspension torn down on both sides. The broad and round ligaments were plicated in front of the uterus, thus closing the hernial opening and shortening the uterine supports.

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Society Transactions

NEW YORK OBSTETRICAL SOCIETY

MEETING OF MAY 13, 1941

The following papers were presented:

Adenomyosis Interna Uteri as a Cause of Uncontrollable Atony and Hemorrhage Following Cesarean Section for Sacculation Pregnancy. Dr. Nelson B. Sackett. (For original article, see page 894.)

Functional Studies on the Vascular System of the Kidney in Normal Pregnancy and in Late Toxemia. Dr. Howard C. Taylor, Jr., and Dr. Irwin Wellen (by invitation). (Will be published in a later issue.)

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF APRIL 18, 1941

The following papers were presented:

The Evaluation of the Several Types of Cesarean Section and Their Indications. Dr. Edward A. Schumann, Philadelphia, Pa. (by invitation).

Indications for the Schumann Type of Cesarean Section. Dr. Walter W. Coen.

MEETING OF MAY 16, 1941

The following papers were presented:

Role of Carbon Dioxide in Resuscitation at Birth After Asphyxia and After Nembutal Anesthesia. Drs. W. F. Windle (by invitation) and R. F. Becker. (For original article, see page 852.)

Roentgen Pelvimetric Analysis of Walcher's Position. Drs. Harold M. Brill, and Gerhard Danelius. (For original article, see page 821.)

PITTSBURGH OBSTETRICAL AND GYNECOLOGICAL SOCIETY

ANNUAL MEETING, MAY, 24, 1941

The following paper was presented:

The Present Status of Endocrinology as It Pertains to Obstetrics and Gynecology. Dr. Robert T. Frank, New York, N. Y., by invitation.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Endocrinology

Kosakae, Kanzaki, and Kusano: The Quantity of Sexual Hormone Discharged in the Urine of Pregnant Women After Castration, Jap. J. Obst. & Gynec. 23: 174, 1940.

In a patient whose both ovaries had been removed, the authors studied the amount of follicular and sexual hormone passed in the urine from six to nine days every month beginning with the sixth month of pregnancy. They continued these observations into the puerperium when daily observations were made. It was found that the results were identical with those observed in normal pregnant women. This is considered by them evidence that the follicular hormone is produced in the placenta.

J. P. GREENHILL.

Furuhjelm, M.: The Excretion of Estrogenic and Androgenic Substances in the Urine of Women, Acta. obst. & gynec. Scandinav. 20: 1, 1940.

The excretion of estrogenic and androgenic substances was determined in two-day lots of urine on 14 healthy women and on 10 women with myomas of the uterus. The curves of the 14 healthy women revealed a typical configuration. The excretion of estrogenic substances showed one, and occasionally two, pronounced peaks. A marked decrease in the estrogenic excretion occurred during menstruation. The estrogenic activity of the urine for two days varied between 20 I.U. and 400 I.U. of estrone. During the ovarian cycle, the healthy woman excretes estrogenic substances equivalent to 1,100 I.U. of estrone. In 10 out of these 14 patients, there was no decrease in the androgenic secretion during menstruation. There was a tendency to parallelism between the excretion of androgenic and estrogenic substance during the intermenstruum. Similar conditions were found in the curves of the 10 women with myomas.

The author also investigated 2 castrated women. He could find no estrogenic substance in the urine up to two weeks after castration. Androgenic substances were found in the same amounts after abortion as before and in approximately the same amounts in normal women.

J. P. GREENHILL.

Corner, George W.: The Rate of Secretion of Estrogenic Hormones by the Ovaries of the Monkey, Macaca Rhesus, Bull. Johns Hopkins Hosp. 67: 407, 1940.

The rate of secretion of estrogenic hormone by the ovaries of the young adult rhesus monkey (weighing 4 to 5 kilograms) is estimated tentatively as equivalent to about 200 International Units (20 gamma) of estrone daily.

Multiplying this figure by a factor of 15, to allow for the proportionate weight, the rate of production of estrogenic hormone by the ovaries of the human female

is roughly estimated as the equivalent of 3,000 I.U. (300 gamma) of estrone daily. This calculation is not very far from an estimate, based on clinical trials by W. M. Allen, of 4,200 I.U. daily.

C. O. MALAND.

Fevold, H. L.: Synergism of the Follicle Stimulating and Luteinizing Hormones in Producing Estrogen Secretion, Endocrinology 28: 33, 1941.

To extend earlier observations of the synergism of the two pituitary gonadotropic hormones (FSH and LH) in initiating secretion of estrogen from the ovaries, Fevold used extracts prepared by previously described methods from sheep pituitaries on normal immature rats.

He concludes that follicle-stimulating hormones are the primary factor in the production of estrogen in the rat, in that it initiates secretory activity. Luteinizing hormones alone cannot initiate, but augment the action of follicle-stimulating hormones in the mechanism of estrogen secretion. The reverse has been shown to be true for the secretory activity of the male gonad.

The possibility of preparing follicle-stimulating hormone extracts free from subminimal amounts of luteinizing hormones is discussed. Uterine and ovarian weights as a method of standardizing pituitary extracts is questioned, as the weight changes of the uterus and ovaries obtained with unfractionated extracts are not an index of the amounts of follicle-stimulating hormones and luteinizing hormones present but rather an expression of the relative proportions of the two.

CLAUDE J. EHRENBERG.

Hoffmann, Fr.: Investigation of Formation of Female Ovarian Hormones in the Adrenal Cortex, Zentralbl. f. Gynäk. 64: 1075, 1940.

Hoffmann studied the corpus luteum and follicle hormones of the adrenal cortex of female, male, and castrate male animals. The extract of the cortex was injected into castrated dogs, and the Robson modification of the Corner-Allen test was used. Extract of 250 Gm. of bovine adrenal cortex gave a maximal corpus luteum effect on the dog endometrium, characteristic of the sixth to eighth day of pseudopregnancy. Extract of 180 Gm. gave a 2-plus reaction; extract of 80 Gm. a positive or doubtful reaction. The reaction to the injection of steer adrenal cortex extract had half the corpus luteum effect compared with the bovine extract. Oxen showed a still weaker effect.

To determine follicle hormone effect, castrated mice were injected with the extract and amounts representing 30 Gm. of adrenal cortex were necessary to produce estrus effect equivalent to that of 1 I.U. of estrone. In comparison, 200 Gm. of adrenal gland and 100 Gm. of ovary are equivalent in producing the effect of 1 Corner unit. As the adrenal cortex is only 20 to 25 per cent of the mass of the gland, its relative corpus luteum potency appears to be higher. Hoffmann also found 1 unit estrone in 25 to 30 Gm. of adrenal cortex.

The author concludes that the adrenal cortex may be considered as accessory sexual glandular tissue whose pathologic significance lies in its ability to produce male and female sex hormones in great quantity in masculinizing and feminizing tumors.

R. J. WEISSMAN.

Tscherne, E.: Contribution to the Etiology of Glandular (Endometrial) Hyperplasia, Zentralbl. f. Gynäk. 64: 1474, 1940.

The author discusses briefly the theories of persistent follicle hormone and pituitary-midbrain effects in maintaining endometrial hyperplasia. In his opinion in these cases, the hypophysis has lost its ability to respond to the stimulus of peak circulating hormone with a response of producing the luteinizing prolan-B. In other words the difficulty is of central origin. The effect of large doses of follicle hormone in inhibiting the menorrhagia of these cases is a direct endo-

metrial effect into which the hypophyseal mechanism does not enter as evidenced by the persistence of the hyperplasia. Several interesting cases are presented.

An 18-year-old girl had been treated in the past with corpus luteum, anterior pituitary, and curettage with varying success. Biopsy showed hyperplastic endometrium. Stilbestrol was given in 3 daily doses, 5, 10, and 15 mg., and the bleeding stopped after the third dose only to begin again eight days later, when biopsy again revealed the persistence of the hyperplasia.

A 47-year-old woman, bleeding fourteen days after a two months' amenorrhea, ceased flowing after a third daily dose of 100,000 I.U. of progynon B. Eight days later biopsy showed persistent hyperplastic endometrium.

A woman, 26 years old (menarche at 13, normal 28-day cycle), was shot in the head. Radiographs showed the slug lying directly behind the sella turcica. After two days of unconsciousness the patient slowly recovered but developed a Korsakoff's psychosis. Because of a homonymous hemianopia, descending optic atrophy, and mild facial paresis it was concluded that the projectile had passed in close proximity to the pituitary, causing a hematoma which had injured either the vegetative centers related to the pituitary or their hypophyseal connections. At any rate a 6-month period of amenorrhea followed the accident and the patient gained 22 kilograms. In a period of seven days 42,000 R.U. doses of prolan were given. Eleven days later a five-day flow occurred. No biopsy was done at this point. The author reconciles the result of this medication with Westmann's work on hypophysectomized animals who undergo follicular atrophy. Reactivation is possible by administration of chorionic hormone because this hormone in turn is activated by the gonadotropic hormone not affected by the operation. In the author's case menstruation was regularly produced at will eleven or twelve days after a series of doses of prolan. At the beginning of each of the menses of December and January, 1940, biopsies were done. In December glandular hyperplasia was found, i.e., pituitary midbrain connections were reestablished, but follicle hormone still blocked from affecting the midbrain. In January, thirteen months after the accident, a normal menstruating endometrium was found indicating restoration of central sensitivity to follicle hormone and ability of the midbrain to effect stimulation of luteinizing (prolan B) hormone.

R. J. Weissman.

Jeffcoate, T. N. A.: Oestrogenic Hormone Therapy, Brit. M. J. 2: 671, 1939.

Estrogens, chemical substances that can promote estrus, in animals, can be obtained as estradiol, esterone, and estriol in human tissues and body fluids, believed to be produced as estradiol, which is secreted by the granulosa cells in the nonpregnant, and the placenta in pregnant females. Esterone and estradiol are more commonly used for therapeutic purposes as the benzoate or other esters dissolved in oil. Biethyl-stilbestrol (stilbestrol) is a synthetic product available for clinical use.

Diminished secretion of estradiol in the adult usually leads to menopausal symptoms, in youth, when the ovary has never functioned, to amenorrhea, oligomenorrhea, under-development of breasts and other sex characteristics. Endometrial biopsy shows atrophic endometrium and vaginal smears show fewer and smaller epithelial cells than normal.

Undoubtedly a large percentage of cases of menopausal symptoms can be eliminated by administration of estrogens. Dosage varies considerably, and is determined by trial. With symptoms controlled, smaller doses are needed. Gradual reduction is necessary.

Senile vaginitis and kraurosis vulvae may be cured with estrogens. In the former injection of 5 mg. twice weekly is recommended and the patient is usually symptom free in two to three weeks. Small doses should be continued for two or three months. Kraurosis vulvae requires more prolonged therapy. In gonococcal vaginitis, 0.1 mg. of esterone should be injected every one to two days and given orally 2 to 3 times daily.

Genital hypoplasia may be due to an estrogenic hormone deficiency or an inherent defect in the organ rendering it insensitive to hormone administration. In

the former, administration of these principles will yield complete development; in the latter they are valueless. It is impossible to foretell whether the uterus will or will not respond to hormones.

Estrogen therapy for amenorrhea depends on the "estrin withdrawal hemorrhage" reaction. If it is not a true menstruation, the endometrium is in a nonsecretory phase. It is estimated that 25 to 30 mg. of estradiol benzoate are necessary to produce such bleeding. The effect is obtained only as long as treatment is continued unless the ovaries are capable of spontaneous function.

Rarely, if ever, will administration of hormones bring about premature termination of a normal pregnancy. Four milligrams of estradiol benzoate every eight hours for eight days are given for missed abortions. Quinine and pituitary induction are given on the fifth and eighth days if necessary. The author reports with this therapy 80 per cent of success in his cases.

That uterine inertia is a deficiency of estrogenic substance and may be overcome with hormone therapy is a supposition and without proof.

Estrogens stimulate development of breast glandular tissue and are of use in underdevelopment, but breasts will atrophy when stimulus is discontinued unless ovarian function is adequate. Chronic mastitis or involutionary mastitis is benefited by estrogenic therapy.

Estrogens do not cause secretion of milk; a prolactic function of the anterior pituitary is inhibited by estrogens. Large amounts of estradiol injected during the puerperium inhibit lactation and relieve breast engorgement.

So far no clinical evidence has shown that estrogens in ordinary dosages have brought about neoplastic changes. Most harmful effect of estrogenic therapy is depression of ovarian activity. A warning against prolonged treatment in young women is given.

Stilbestrol, a synthetic substitution, may be given orally as effectively as parenterally. One milligram of it is equivalent to 1 mg. of estradiazol benzoate, and has proved of value in all of the above-mentioned conditions. The disadvantage is that it produces nausea and malaise when given in large doses.

FRED L. ADAIR AND JOHN R. KIGHT.

Scherf, David: The Respiratory and the Circulatory System in Females With Ovarian Dysfunction, Ann. Int. Med. 13: 1414, 1940.

Treatment with estrogenic hormones appears to have a beneficial effect upon disturbances in the respiratory and circulatory system of women at the menopause or under other conditions of ovarian hypofunction.

In 38 women, some of whom were being mistakenly treated for angina pectoris, myocarditis, or coronary sclerosis, the author was able to demonstrate changes in the electrocardiogram which might rightfully be ascribed to ovarian hypofunction, since they disappeared after administration of estrogenic hormone.

In every case, treatment with adequate dosages of estrogenic hormones was followed by very rapid relief of symptoms and the return of the electrocardiogram to normal. In some cases, the electrocardiographic changes vanished within eight days after the administration of as little as 1,000 to 2,000 International Units of estrogen daily. In other cases, the hypodermic injection of 10,000 to 50,000 units, two to three times a week for three to four weeks, was necessary for improvement.

The dyspnea of ovarian dysfunction, particularly at the menopause, occurs independently of effort and may be present when the patient is resting quietly.

The normal disturbances in respiratory and circulatory function at the time of the menopause may represent a most profound danger for women who already harbor an organic heart lesion. Such valvular lesions, or hypertension, quiescent for years, may suddenly produce decompensation when the middle forties are reached. The heart dilates quickly, and cardiac asthma, pulmonary edema, and peripheral congestion appear.

This event is not rare and it can be avoided. The estrogenic function of every cardiac patient should be continuously controlled, especially if the patient is at the age when disturbances of the menopause are likely to occur. Early prophylactic treatment with estrogenic hormones may save many lives.

J. P. GREENHILL.

Mazer, Charles, Israel, S. Leon, and Ravetz, Elkin: The Synthetic Estrogen Stilbestrol, J. A. M. A. **116:** 675, 1941.

The authors review their experiences in 189 cases with stilbestrol. They feel that the biologic potency of stilbestrol when given hypodermically is five times greater than that of estrone and equal to that of estradiol benzoate. The ratio between the oral and the hypodermic doses of stilbestrol is 5 to 1 in the human being, as well as in the rat, in contrast to a ratio of 20 to 1 in terms of the rat unit for the natural estrogens. It is suggested that injections of adequate quantities of stilbestrol twice weekly is sufficient for clinical purposes.

One hundred and twenty-two patients receiving 0.2 to 5 mg. daily by the oral route or every fourth day parenterally showed complete relief in 68 per cent, partial relief in 27.9 per cent, and no relief in 4 per cent of the cases. Occasional cases of sporadic uterine bleeding were encountered as a result of the withdrawal of stilbestrol. In amenorrhea the authors gave 50,000 rat units in 5 divided doses in 15 women, and menstrual-like bleeding was produced in six of seven attempts. They were also successful in suppressing lactation by giving 3 to 10 mg. of stilbestrol daily for a period of from two to four days. Successful treatment in 50 per cent of the cases of migraine resulted from the use of stilbestrol. It was also effective in the treatment of juvenile vaginitis. Stilbestrol is also useful in reducing the insulin requirements of diabetics, but it has no effective place in the treatment of diabetes mellitus unless a corresponding menopausal syndrome is present.

The drug had to be discontinued in 22.2 per cent of the cases because of toxic symptoms, chief of which were nausea and vomiting, epigastric pain, and abdominal distress. The smaller the dose the less is the toxic effect. Tissue damage in the human being resulting from the administration of relatively large doses of stilbestrol given over a long period of time is not demonstrable by physical examination, and by ordinary laboratory means, although animals do show some kidney, liver, and adrenal gland changes.

WILLIAM BERMAN.

Weinstein, Weed, Collins, Lock, and Schlosser: The Effect of Diethyl Stilbestrol Dipropionate on Endometrial Transplants, Endocrinology **27:** 903, 1940.

To determine the probability of successfully transplanting estrogenically primed endometrium and to study the effect of continued estrogenic administration on these transplants, the authors used diethyl stilbestrol dipropionate on adult virgin chinchilla rabbits. Two groups of animals, each of which except the controls received daily injections of 12,500 I.U. of stilbestrol until a total of 600,000 I.U. had been used, were laparotomized. Extreme hypertrophy of the uterine cornua, hypertrophy of the vagina, but no effect on the ovaries and oviducts were consistently noted. Portions of excised uterine cornua were sutured to the mesentery of the small bowel and the abdominal peritoneum. The animals were continued on the preoperative estrogen treatment, Group I receiving an additional dosage of 375,000 I.U., and Group II receiving an additional dosage of 525,000 I.U.

All transplants were successful with viable endometrial tissue. Cyst formation in the endometrium was constant even in the controls. The size of the cysts was in direct proportion to the amount of estrogen used as was vasodilatation, the only change demonstrable, in the surrounding host tissue. Microscopic examination of the transplant tissue revealed no invasive tendency or increased cellular activity, but because of the stimulating effect of the estrogen, the authors caution against the use of large doses of estrogens postoperatively, in women castrated to decrease symptoms of endometriosis.

CLAUDE J. EHRENBERG.

Joel, C. A.: The Question of the Stilbens, a Synthetic Follicular Hormone, Monatschr. f. Geburtsh. u. Gynäk. **111:** 63, 1940.

Stilbestrol which is cheaper than follicular hormones may replace the latter in the opinion of the author. Experimental research has proved a qualitative simi-

larity between stilbestrol and the follicular hormones. Stilbestrol is particularly effective when taken by mouth. There is, however, no cancer-producing effect.

J. P. GREENHILL.

Von Konrád, E.: Treatment of Metropathia Hemorrhagica With Testosterone Propionate, Zentralbl. f. Gynäk. 64: 1135, 1940.

The author discusses his results in the treatment of metrorrhagia in 17 patients —the oldest 19 years of age. Five daily doses of 25 mg. testosterone were administered. All but two patients had ceased bleeding by the fifth injection. These two required 9 and 10 doses. Characteristically there followed varying periods of amenorrhea after which the patients again menstruated regularly. The favorable effect of the male hormone is attributed to its influence on luteinization. Von Konrád favors the routine use of male hormone in juvenile menorrhagia and in noncarcinomatous uterine bleeding of other etiology.

R. J. WEISSMAN.

DeBarros, Rubins Monteiro: Use of Testosterone Propionate in Hemorrhage Due to Myoma Uteri, Rev. de gynec. e d' obst. 1: 394, 1940.

The author reports a case of myoma uteri with severe hemorrhage in which he employed testosterone propionate in an effort to improve the patient's condition before operation. He feels that this substance can be utilized preoperatively with advantage to control the hemorrhage due to fibromyoma.

MARIO A. CASTALLO.

Huber, Carl P., and Davis, M. Edward: The Clinical Use of Gonadotropic Hormone From Pregnant Mares' Serum, Surg., Gynec. & Obst. 70: 996, 1940.

The administration of gonadotropic hormone from pregnant mares' serum has been followed by pregnancy in previously sterile patients in whom anovulatory menstrual cycles have been demonstrated.

This gonadotropic hormone has proved clinically effective in some cases of acyclic uterine bleeding associated with evidence of continued endometrial proliferation.

Amenorrhea resulting from inadequate ovarian activity has responded to this gonadotropic hormone by the occurrence of uterine bleeding.

No untoward effects have been demonstrated either locally or systemically following several hundred intramuscular and intravenous injections of this hormone.

Further carefully controlled clinical observations are necessary definitely to establish the therapeutic value and indications for the use of gonadotropic hormone from pregnant mares' serum.

WILLIAM C. HENSKE.

Lawrence, Ch. H., and Moulyn, Adrian C.: The Menopause: A Hormonic and Therapeutic Study, New England J. Med. 224: 845, 1941.

In only a small minority of women are the symptoms associated with "the change of life" sufficiently severe to compel them to consult a physician.

In their studies the authors found that a test for prolan was positive in only 48 of 100 women coming to the clinic for severe symptoms, in 81 per cent the symptoms being particularly those of vasomotor instability. Of these, 90 per cent were definitely benefited by adequate treatment with estrin. In the prolan negative group, however, estrin caused improvement in only 25 per cent, whereas simple psychotherapy or sedation brought relief in 80 per cent.

No relation was evident in either group between the presence or absence of estrin alone and the character or severity of symptoms. A predominance of vasomotor symptoms is suggestive of an overactive prolan production, but treatment with estrin should not be instituted until urinary assay proves that prolan is excreted.

If treatment with estrin is indicated, it should be given in effective amounts; the effective dosage, however, in any patient is an individual equation.

HUGO EHRENFEST.

Pattee, C. J., Venning, E. H., and Browne, J. S. L.: The Effect of Estrogens on the Pregnandiol Output During the Menstrual Cycle, Endocrinology **27**: 721, 1940.

The effects on the menstrual rhythm of injections of estrogen, as recorded by other authors, are reviewed. Excretion of pregnanediol was studied in three women receiving estradiol benzoate (20,000 to 80,000 I.U.) during menstrual cycles. Decreased pregnanediol output was noted in all such cycles. The findings confirm the work of other authors, that, given in the luteal phase, estrogens will depress the urinary excretion of pregnanediol. The mechanism of the phenomenon is postulated.

CLAUDE J. EHRENBERG.

Herrnberger, K.: Oral Potency of Estradiol and Progesterone, Zentralbl. f. Gynäk. **65**: 13, 1941.

The author administered estradiol in tablet form in doses up to 450 mg. without any observable proliferation effect on the endometrium of castrate women. In alcoholic solution, however, doses of 180 mg. estradiol were able to produce a proliferative phase in the endometrium. Herrnberger was unable to find any effect from large doses of oral progesterone. Pregninolone in oral dosage, however, was capable of producing a secretory phase in proliferated endometrium.

R. J. WEISSMAN.

Lawrence, Charles H., and Werthessen, Nichoload T.: The Endocrine Dyscrasia of Acne Vulgaris in Women, Endocrinology **27**: 755, 1941.

The urinary androgen-estrogen ratios of eight normal women and eight women with acne were determined in forty-eight-hour specimens taken between the sixteenth and twentieth days of the menstrual cycle. The technique of the assay methods and the statistical and mathematical handling of the data are described in detail.

A significant increase in the ratio of androgens to estrogens measured as estrone equivalents, through abnormal lowering in estrogens was demonstrated in the acne group. This aberrant ratio is considered of more etiologic significance than the decrease of estrogen excretion alone. The findings from a clinical point of view are thought to agree with the biologic evidence concerning acne.

CLAUDE J. EHRENBERG.

Bauer, W.: Clinical Results of Follicle Hormone Therapy, Zentralbl. f. Gynäk. **64**: 1682, 1940.

The author attributes the low incidence of failures in his own experience with follicle hormone therapy (12 in 374 cases), to his careful selection of cases. Juvenile metrorrhagia and polymenorrhea with hypermenorrhea responded with uniform good results. New uses for follicle hormone were found in treating fissured nipples and also urinary incontinence of young girls, although the rationale is not thoroughly understood.

R. J. WEISSMAN.

Miotti, Tito: Changes in the Genital Apparatus of the Female Guinea Pig Induced by the Action of Prostatic Extracts, Ginecologia **19**: 141, 1941.

The author attempted to prove the presence or absence of hormonal activity in extracts of the prostate gland. Normal and castrate female guinea pigs were treated with these extracts.

The author concludes that there is no evidence of any hormonal effect of prostatic extracts upon the genital tract of the female guinea pig. In some instances there was observed slight vasodilatation among the smaller uterine veins.

CLAIR E. FOLSOME.

Item

American Board of Obstetrics and Gynecology

The written examination and review of case histories (Part I) for Group B candidates will be held in the various cities of the United States and Canada, on Saturday, January 3, 1942, at 2:00 P.M. Formal notice of the place of examination will be sent each candidate several weeks in advance of the examination date. No candidate will be admitted to examination whose examination fee has not been paid at the Secretary's Office. Candidates who successfully complete the Part I examination will proceed automatically to the Part II examination held in June, 1942.

Candidates for *reexamination* in Part I (written paper and submission of case histories) must request such reexamination by writing the Secretary's Office not later than November 15, 1941. Candidates who are required to take reexaminations must do so before the expiration of three years from the date of their original examination.

The general oral and pathological examinations (Part II) for all candidates (Groups A and B) will be conducted by the entire Board, meeting at Atlantic City, N. J., in June, 1942, immediately prior to the annual meeting of the American Medical Association.

Application for admission to Group A, Part II, examinations must be on file in the Secretary's Office not later than March 1, 1942.

As previously announced in the Board booklet, this fiscal year (1941-1942) of the Board marks the close of the two groups of classification of applicants for examination. Thereafter, the Board will have only one classification of candidates, and all will be required to take the Part I examinations.

For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

Books Received

ANALGESIA OBSTETRICA, el sueno crepuscular barbiturico en el parto. By Juan Leon, Professor adjunto de Clinica Obstetrica de la Faculdad de Ciencias Medicas de Buenos Aires, etc. 574 pages, 169 illustrations. El Ateneo, Buenos Aires, 1941.

DIE TAEGLICHE GYNAEKOLOGISCHE SPRECHSTUNDE. Von Dr. M. Rodecurt, Frauenarzt. 308 Seiten, 3 Abbildungen. Georg Thieme, Leipzig, 1941.

THE MARCH OF MEDICINE. New York Academy of Medicine Lectures to the Laity. 1940. Columbia University Press, New York, 1941.

ARCHIVOS DE LA CLINICA E INSTITUTO DE ENDOCRINOLOGIA. Director, Professor J. C. Mussio Fournier. Tomo I, Fasc. 1. and 2. (1937-1940) mprenta "Rosgal." Montevideo, Calla Cerro Largo, 1941.

THE THERAPEUTICS OF INTERNAL DISEASES. Supervising editor: George Blumer, Clinical Professor of Medicine, Yale University School of Medicine, etc., Associate Editor: Albert J. Sullivan, Adjunct Clinical Professor of Medicine, George Washington and Georgetown Medical Schools, etc. Volume IV. 791 pages, and Volume V. 765 pages, both illustrated. D. Appleton-Century Co., New York, 1941.